ORGANIC SYNTHESES

I

ACROLEIN ACETAL

$$ClCH_2CH_2CH(OC_2H_5)_2 + KOH \rightarrow CH_2{=}CHCH(OC_2H_5)_2 + KCl + H_2O$$

Submitted by E. J. Witzemann, Wm. Lloyd Evans, Henry Hass, and E. F. Schroeder.
Checked by Frank C. Whitmore and Harry T. Neher.

1. Procedure

To 340 g. (6 moles) of dry, powdered potassium hydroxide (Note 1) in a 500-cc. short-neck round-bottom flask (Note 2) is added 167 g. (1 mole) of β-chloropropionaldehyde acetal (p. 26). The mixture is shaken vigorously and attached at once to a 3-bulb Glinsky, or other suitable column, connected to a water condenser set for distillation. The flask is heated in an oil bath at 210–220° until nothing more distils (Note 3). The distillate is transferred to a separatory funnel and the lower aqueous layer is removed. The acrolein acetal is dried over 10 g. of potassium carbonate, filtered and distilled from a modified Claisen flask (Org. Syn. 1, 40). The yield is 98 g. (75 per cent of the theoretical amount) of a product which boils at 122–126°.

2. Notes

1. The powdered potassium hydroxide should pass a 60-mesh sieve (24 per cm.). The dryness of the powder is of the utmost

importance. Water must be avoided as much as possible. Therefore, the potassium hydroxide should be fused at 350° for two hours and then pulverized as rapidly as possible. A 24-cm. (10-in.) disk pulverizer having a capacity of about 200 g. per minute is recommended. If the potassium hydroxide is not fused before pulverizing, the yield of acetal drops to about 60 per cent.

2. The concentrated potassium hydroxide left at the completion of the reaction attacks the glass rapidly. For this reason iron retorts made from 10-cm. (4-in.) pipe should be used when many runs are to be made.

3. A large low-boiling fraction indicates too much moisture in the potassium hydroxide used. See Note 1.

3. Methods of Preparation

Acrolein acetal has always been prepared by treatment of β-chloropropionaldehyde acetal with dry, powdered potassium hydroxide.[1]

[1] Wohl, Ber. **31**, 1798 (1898); Witzemann, J. Am. Chem. Soc. **36**, 1911 (1914); Spoehr and Young, Carnegie Inst. Washington Yearbook, **25**, 176 (1925 1926); Expt. Sta. Record, **57**, 817 (1927) [C. A. **22**, 2368 (1928)].

II

α-AMINOISOBUTYRIC ACID

$$CH_3COCH_3 + NaCN + NH_4Cl \rightarrow (CH_3)_2C(OH)CN + NaCl + NH_3$$

$$(CH_3)_2C(OH)CN + NH_3 \rightarrow (CH_3)_2C(NH_2)CN + H_2O$$

$$(CH_3)_2C(NH_2)CN + 2H_2O + 2HBr \rightarrow (CH_3)_2C(NH_2 \cdot HBr)CO_2H + NH_4Br$$

$$(CH_3)_2C(NH_2 \cdot HBr)CO_2H + C_5H_5N \rightarrow (CH_3)_2C(NH_2)CO_2H + C_5H_5N \cdot HBr$$

Submitted by H. T. CLARKE and H. J. BEAN.
Checked by C. S. MARVEL and C. F. BAILEY.

1. Procedure

A FILTERED solution of 200 g. (3.75 moles) of ammonium chloride in 500 cc. of water is placed in a 1-l. round bottom flask. The flask is surrounded by an ice bath and cooled to 5–10°. A solution of 175 g. (3 moles) of acetone in 500 cc. of ether is added with stirring (Note 1). Then a solution of 160 g. (3.2 moles) of sodium cyanide in 350 cc. of water is added, with stirring, at such a rate that the temperature never exceeds 10° (Note 2).

The reaction mixture is stirred for one hour after all the cyanide has been added and then is allowed to stand overnight. The ether layer is separated and the aqueous liquor is extracted with six 300-cc. portions of ether. The ether extracts are combined and the ether is distilled. The residue, which consists mainly of acetone cyanohydrin, is diluted with 800 cc. of methyl alcohol. The solution is cooled and saturated with ammonia gas (Note 3). The reaction mixture is allowed to stand for two or three days

(Note 4) and the excess ammonia is expelled by a current of air. The methyl alcohol is removed by distillation as completely as possible, and 600 cc. of water is added to the residue. Then 1000 g. of 48 per cent hydrobromic acid is added and the mixture is refluxed for two hours.

The hydrobromic acid is distilled under reduced pressure on a steam bath. The residue is treated with 400–500 cc. of water, and the solution is again concentrated under reduced pressure to remove as much hydrobromic acid as possible (Note 5).

The residue is dissolved in fifteen to twenty times its weight of methyl alcohol (Note 6), filtered and an excess of pyridine (Note 7) is added. The free amino acid separates on standing overnight. It is collected on a Büchner funnel, washed thoroughly with methyl alcohol and dried. The yield is 92–102 g. (30–33 per cent of the theoretical amount). If a pyridine-free product is desired, it is dissolved in 200 cc. of warm water, filtered and the filtrate poured into 2 l. of methyl alcohol (Note 8). There is less than 10 g. of product in the mother liquors. It may be isolated by evaporating to dryness, washing with methyl alcohol and purifying by reprecipitation in the same way.

2. Notes

1. Vigorous stirring is necessary to obtain the best results.

2. The reaction temperature may rise to 15° without lowering the yield. If the temperature falls to 0°, the reaction does not take place readily.

3. The excess of ammonia is necessary to cause the formation of the aminonitrile from the acetone cyanohydrin formed in the first stage of the process.

4. In some runs this time was only twenty-four hours and no serious diminution of the yield was noted.

5. After addition of the water and subsequent evaporation almost to dryness it is well to add another small portion of water (25–75 cc.) and again evaporate to dryness to insure the complete removal of hydrobromic acid. This should be done several times if necessary.

6. The amount of methyl alcohol should not exceed 3 l., otherwise the amino acid will be precipitated incompletely. Long stirring in the cold may be necessary to effect complete solution, though apparently no difficulty is encountered if the residue does not dissolve completely.

7. The minimum amount of pyridine necessary is determined by the amount of hydrobromic acid remaining in the residue. An excess of pyridine does no harm. If it is desired to use the minimum amount, pyridine is added in small portions until the solution is neutral to Congo red, and then an additional 250 g. is added.

8. A further small quantity may be obtained by evaporating the mother liquor to a small volume on a steam bath, allowing it to crystallize, and washing the crystals with methyl alcohol.

3. Methods of Preparation

The only satisfactory method of preparing α-aminoisobutyric acid is the Strecker synthesis [1] in one or another of its modifications.[2] The process of isolating the product by treating an alcoholic solution of the hydrobromide with pyridine is essentially the same as that developed for glycine.[3]

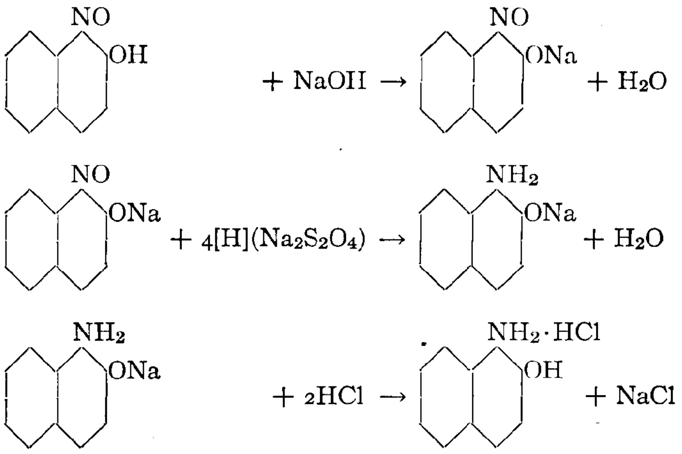
[1] Strecker, Ann. **75**, 28 (1850).

[2] Tiemann and Friedlander, Ber. **14**, 1970 (1881); Marckwald, Neumark, and Stelzner, Ber. **24**, 3283 (1891); Gulewitsch, Ber. **33**, 1900 (1900); Hellsing, Ber. **37**, 1923 (1904); Gulewitsch and Wasmus, Ber. **39**, 1184 (1906); Zelinsky and Stadnikoff, Ber. **39**, 1726 (1906).

[3] Org. Syn. **4**, 31 (1925).

III

1-AMINO-2-NAPHTHOL HYDROCHLORIDE



Submitted by J. B. CONANT and B. B. CORSON.
Checked by F. C. WHITMORE and A. L. OSTERHOF.

1. Procedure

IN an 8-l. (2-gal.) earthenware crock, equipped with a mechanical stirrer and a tube for introducing steam, are placed 240 g. (1.39 moles) of nitroso-β-naphthol (from 200 g. of β-naphthol, Org. Syn. **2**, 61) (Note 1), 1.5 l. of water, and 300 cc. of 5 N sodium hydroxide. The lumps are broken up with a rod and the mixture is stirred for about thirty minutes. At the end of this time, practically all of the nitroso compound is dissolved and 1200 cc. of 5 N sodium hydroxide is added. Steam is passed in until the temperature of the mixture is 35°, and then the steam

is shut off and 600 g. of technical sodium hydrosulfite (at least 85 per cent pure) is added while the solution is being stirred. The solution is stirred continuously for five minutes while the temperature rises to 60–65°, and then for one minute at five-minute intervals during one-half hour. At the end of about fifteen minutes the solution becomes clear and light yellow in color. A small amount of black scum floats on the surface.

The solution is now cooled to 20° by the addition of about 1 kg. of ice, and 500 cc. of technical concentrated hydrochloric acid (sp. gr. 1.16) is added with stirring. This precipitates the aminonaphthol as a voluminous, almost white precipitate (Note 2) which is collected on two 20-cm. Büchner funnels. It is rapidly pressed as free from mother liquor as possible and transferred quickly (Note 3) to an 8-l. (2-gal.) crock containing 2.5 l. of water and 250 cc. of technical concentrated hydrochloric acid. The large lumps are broken up with a rod, steam is passed in, and the stirrer is started. Steam is introduced at such a rate that a temperature of 85–90° is reached within ten minutes; the mixture is stirred at this temperature for one hour longer. The hot mixture is then filtered through a 15-cm. Büchner funnel and the filtrate is cooled to 35–40° in an ice bath.

The claret-colored solution (5200-5800 cc.) is filtered through a fluted filter paper in a 15-cm. funnel into 1200 cc. of concentrated hydrochloric acid in an 8-l. bottle. The aminonaphthol hydrochloride starts to precipitate immediately. The mixture is allowed to stand for at least two hours with occasional agitation to insure complete precipitation. The hydrochloride is collected on a 15-cm. Büchner funnel and washed successively with three small portions of 20 per cent hydrochloric acid and three 50-cc. portions of ether (Note 4). It is then dried in the air in thin layers on filter paper (Note 5). The yield is 180–200 g. of anhydrous material (Note 6) (66–74 per cent of the theoretical amount based on 200 g. of β-naphthol). The hydrochloride is unstable; in solution it decomposes rapidly, but this decomposition can be largely prevented by the addition of

sodium bisulfite. The dry solid slowly changes and should be used within a few weeks of its preparation.

2. Notes

1. It is usually not convenient to dry the nitroso-β-naphthol. The amount given in these directions corresponds to 200 g. of β-naphthol and the yield is calculated on this basis. The nitroso-β-naphthol dissolves in one mole of sodium hydroxide, forming a green solution. There is left in suspension a small amount of amorphous brown material which it is unnecessary to remove.

2. The amounts of sodium hydroxide, sodium hydrosulfite and hydrochloric acid used are such that complete precipitation of the aminonaphthol results at this point. It is well to test for complete precipitation, however, by adding a few drops of alkali to one portion of the filtrate and a little acid to another.

3. The aminonaphthol is very sensitive to atmospheric oxidation. When first precipitated it is white, but it becomes purple in the air and therefore should be handled rapidly. A small amount of sodium bisulfite may be added at this point to decrease the oxidation, but this is usually unnecessary since some bisulfite from the reduction adheres to the precipitate and this is carried through to the final precipitation.

4. If the material is to be used without being dried, the washing with ether may be omitted.

5. The washing with a little ether greatly facilitates the drying of the product and also produces a somewhat lighter product. In order to obtain the true weight of the material, however, an aliquot sample should be dried over sodium hydroxide under reduced pressure. An air-dried material, when apparently completely dry, contains 10–15 per cent of moisture.

6. The product, as first formed, is a very light purple but darkens on long standing. It may be purified by dissolving in hot water containing sodium bisulfite, filtering and reprecipitating with hydrochloric acid.

3. Methods of Preparation

1-Amino-2-naphthol hydrochloride has been prepared from nitroso-β-naphthol by reduction with ammonium sulfide,[1] or with stannous chloride and hydrochloric acid;[2] from sodium β-naphthol-azobenzenesulfonate (Orange II; β-Naphthol Orange) by reduction with stannous chloride and hydrochloric acid,[3] with zinc and hydrochloric acid,[4] with tin and hydrochloric acid,[5] or with sodium hydrogen sulfide;[6] and by reduction of nitro-β-naphthol with stannous chloride and hydrochloric acid.[7]

1 Stenhouse and Groves, Ann. **189**, 153 (1877); Groves, J. Chem. Soc. **45**, 296 (1884).

2 Groves, J. Chem. Soc. **45**, 296 (1884).

3 Groves, J. Chem. Soc. **45**, 292 (1884); Liebermann and Jacobson, Ann. **211**, 53 (1882); Russig, J. prakt. Chem. (2) **62**, 56 (1900).

4 Zincke, Ann. **278**, 188 (1894).

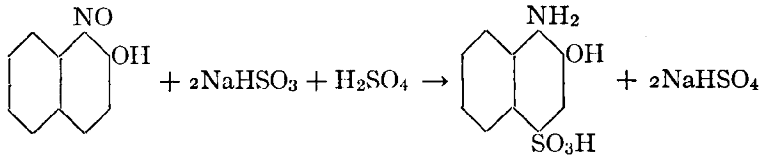
5 Grandmougin and Michel, Ber. **25**, 981 (1892).

6 Groves, J. Chem. Soc. **45**, 294 (1884).

7 Liebermann and Jacobson, Ann. **211**, 48 (1882).

IV

1-AMINO-2-NAPHTHOL-4-SULFONIC ACID



Submitted by Louis F. Fieser.
Checked by F. C. Whitmore and D. J. Loder.

1. Procedure

Three hundred grams of β-naphthol (2.1 moles) is converted into nitroso-β-naphthol (Org. Syn. **2**, 61) (Note 1) and the product is transferred to a 6-l. (1.5 gal.) crock which is wide enough to admit the Büchner funnel (30-cm.) employed. A cold solution of 600 g. (5.8 moles) of sodium bisulfite and 100 cc. of 6 N sodium hydroxide solution in 2 l. of water (Note 2) is used to rinse the material adhering to the funnel into the crock. The mixture is diluted with water to 4–4.5 l. and stirred until solution of the nitroso-β-naphthol is complete (about fifteen minutes). The dark solution is siphoned onto a large Büchner funnel and filtered by suction, thus removing a small amount of tarry material which is always present. The clear, yellowish-brown filtrate is transferred to an 8- to 10-l. wide-mouth bottle, and diluted with water to 7 l. While vigorously stirring the solution, 400 cc. of concentrated sulfuric acid is poured slowly down the walls of the bottle; the mixture is then placed in the hood and protected from the light (Note 3). The temperature rises from 20–25° to 35–40° at once and to about 50° in the

course of two hours, when the reaction is nearly complete. After standing for a total of five hours or more (Note 4), the precipitate, which sets to a stiff paste in the bottle, is collected on a filter. The residue is transferred to a 1-l. beaker and washed with 200 cc. of water. The mixture is filtered and the residue is washed with 300 cc. of water on the filter. The moist material weighs 700–800 g. No appreciable decomposition takes place on drying the product to constant weight at 120°. A light powder of fine, gray needles is thus obtained. The yield is 410–420 g. (82–84 per cent of the theoretical amount based on the β-naphthol used).

2. Notes

1. In preparing nitroso-β-naphthol in the quantity here required it is convenient to use a 7- to 8-l. bottle with an 8- to 10-cm. opening, and equipped with a stirrer of heavy glass rod having four or five right-angle bends which extend to the top of the bottle and which are just small enough to fit the mouth. The bottle is placed in a bucket containing a salt-ice mixture which is stirred occasionally by hand. With this arrangement a temperature of 0° may be maintained without internal cooling.

2. Sodium hydroxide is added to the bisulfite solution in order to neutralize any acid which has not been removed by washing and which would liberate sulfur dioxide and thus cause some reduction of the nitroso compound before the addition product is formed. An excess of alkali, as employed above, aids in the solution of the material.

3. The aminonaphtholsulfonic acid becomes rose colored on long exposure to the light, especially when moist.

4. The time required for the process may be shortened somewhat by adding the sodium bisulfite-sodium hydroxide solution to the suspension of the crude nitroso compound, thus avoiding a long filtration. The amount of water employed in the various operations should be reduced to a minimum, and enough additional sodium hydroxide solution should be used to neutralize

the excess acid present. The product is of a slightly inferior quality and the yield is 4–5 per cent lower.

3. Methods of Preparation

1-Amino-2-naphthol-4-sulfonic acid has been prepared by warming 2-naphthoquinone-1-chloroimide with sodium bisulfite solution;[1] by reduction of 1-benzeneazo-2-naphthol-4-sulfonic acid with stannous chloride and hydrochloric acid;[2] by treatment of 1-amino-2-naphthol hydrochloride with sodium sulfite;[3] and by treatment of nitroso-β-naphthol with sodium bisulfite and hydrochloric acid.[4]

[1] Friedländer and Reinhardt, Ber. **27**, 241 (1894).
[2] Marschalk, Bull. soc. chim. (4) **45**, 660 (1929).
[3] Marschalk, Bull. soc. chim. (4) **45**, 662 (1929).
[4] Schmidt, J. prakt. Chem. (2) **44**, 522 (1891); Böniger, Ber. **27**, 23 (1894).

V

AZOXYBENZENE

$$4C_6H_5NO_2 + 3As_2O_3 + 18NaOH \rightarrow 2C_6H_5N{=}NC_6H_5(\text{=O}) + 6Na_3AsO_4 + 9H_2O$$

Submitted by H. E. Bigelow and Albert Palmer.
Checked by Henry Gilman and H. J. Harwood.

1. Procedure

Sodium arsenite is prepared by dissolving 226 g. (1.14 moles) of powdered arsenious oxide, made into a paste with a little water, in a solution of 275 g. (6.88 moles) of sodium hydroxide dissolved in 600 cc. of water. This solution, diluted with 600 cc. of water, is poured into a 2-l. three-neck flask, provided with a reflux condenser and a mechanical stirrer, and 150 g. (1.22 moles) of freshly distilled nitrobenzene is added (Note 1).

The mixture is refluxed on an oil bath for eight hours with constant and vigorous stirring (Note 2). After removing the oil bath, the reaction mixture is allowed to cool to about 80°, while stirring is continued, and is then transferred to a separatory funnel previously heated to about the same temperature in an oven (Note 3).

The upper layer of oil is separated, run at once into an open vessel and washed with water to which a little hydrochloric acid has been added. Yellow crystals form at once (Note 4), and the yield of azoxybenzene melting at 35.5–36.5° is 102 g. (85 per cent of the theoretical amount) (Note 5).

2. Notes

1. The excess of sodium arsenite and the eight-hour period of heating insure the complete utilization of nitrobenzene. This makes it unnecessary to use steam distillation or other processes for the removal of unreacted nitrobenzene.

Crude nitrobenzene may be used, but a good grade is recommended. When crude nitrobenzene is used, a darker product having a slightly lower melting point is usually obtained.

2. The internal temperature should be about 104°, and the temperature of the bath should not greatly exceed 115°. A smaller flask might be used were it not for the danger of foaming which would result from accidental stopping of the stirrer. If the reaction is interrupted, the oil bath must be removed even though the stirring has been stopped, otherwise, on resumption of stirring, the superheated material may be ejected through the condenser. With these precautions in mind it is unnecessary to have a continuous eight-hour period of heating.

3. In this way the separation is effected at about 60°, and the danger of the solution cooling to a point where sodium arsenate separates is avoided. Should the sodium arsenate separate because of undue cooling, the mixture is heated again with stirring, until the arsenate redissolves. On dilution with sufficient water to keep the arsenate in solution, the oil settles to the bottom and does not separate readily from the liquid. Furthermore, the volume of solution is so large with such dilution that it is less easily handled.

4. The presence of hydrochloric acid accelerates crystallization. Should crystallization be retarded, it is recommended that the oil be seeded with a crystal of azoxybenzene.

5. Recrystallization from 50 cc. of hot 95 per cent alcohol gives 72 g. of azoxybenzene melting also at 35.5–36.5°. However, the recrystallized product is distinctly lighter in color.

6. The solution from which the original oil separated will yield, when diluted with an equal volume of water, a small additional quantity of azoxybenzene. This may be recovered

by extraction with benzene, but the quantity of compound so obtained does not justify this extra procedure.

7. Contrary to the general statement found in the literature, azoxybenzene is somewhat volatile with steam. Therefore, the presence of oil drops in the condenser at the end of the eight-hour period of refluxing is no criterion of unaltered nitrobenzene. Azoxybenzene is easily volatile with steam at 140–150°.

3. Methods of Preparation

Azoxybenzene has been prepared by reduction of nitrobenzene with alcoholic potassium hydroxide,[1] with sodium amalgam,[2] with hydrogen in the presence of lead oxide,[3] with methyl alcohol and sodium hydroxide,[4] with sodium methylate and methyl alcohol,[5] and by electrolytic reduction;[6] by oxidation of azobenzene with chromic anhydride;[7] by treatment of β-phenylhydroxylamine with alkaline potassium permanganate,[8] with nitrobenzene,[9] with mineral acids,[10] and with mercury acetamide,[11] and by oxidation of aniline with hydrogen peroxide,[12] and with acid permanganate solution in the presence of formaldehyde.[13] The procedure described above is a slight modification of one described in the literature.[14]

[1] Zinin, J. prakt. Chem. (1) **36**, 98 (1845).
[2] Alexeyeff, Bull. soc. chim. (1) **1**, 325 (1864).
[3] U. S. pat. 1,451,489 [C. A. **17**, 1969 (1923)].
[4] Lachman, J. Am. Chem. Soc. **24**, 1180 (1902).
[5] Brühl, Ber. **37**, 2076 (1904).
[6] Löb, Ber. **33**, 2332 (1900); Ger. pat. 116,467 (Chem. Zentr. **1901**, I, 149).
[7] Wreden, Ber. **6**, 557 (1873).
[8] Reissert, Ber. **29**, 641 (1896).
[9] Bamberger and Renauld, Ber. **30**, 2278 (1897).
[10] Bamberger and Lagutt, Ber. **31**, 1501 (1898).
[11] Forster, J. Chem. Soc. **73**, 786 (1898).
[12] Prud'homme, Bull. soc. chim. (3) **7**, 622 (1892).
[13] Bamberger and Tschirner, Ber. **32**, 342 (1899).
[14] Loesner, J. prakt. Chem. (2) **50**, 564 (1894).

VI

α-BROMOISOVALERIC ACID

$$(CH_3)_2CHCH(CO_2C_2H_5)_2 + 2KOH \rightarrow (CH_3)_2CHCH(CO_2K)_2 + 2C_2H_5OH$$

$$(CH_3)_2CHCH(CO_2K)_2 + 2HCl \rightarrow (CH_3)_2CHCH(CO_2H)_2 + 2KCl$$

$$(CH_3)_2CHCH(CO_2H)_2 + Br_2 \rightarrow (CH_3)_2CHCBr(CO_2H)_2 + HBr$$

$$(CH_3)_2CHCBr(CO_2H)_2 \xrightarrow{\text{(heat)}} (CH_3)_2CHCHBrCO_2H + CO_2$$

Submitted by C. S. Marvel and V. du Vigneaud.
Checked by Frank C. Whitmore and A. M. Griswold.

1. Procedure

A solution of 200 g. (3.5 moles) of potassium hydroxide in 200 cc. of water is placed in a 2-l. flask fitted with a reflux condenser. The mixture is heated to about 80° and 202 g. (1 mole) of isopropylmalonic ester (Note 1) is added through the condenser over a period of about one hour. The mixture should be shaken well to prevent the formation of two layers. The saponification proceeds rapidly forming a clear solution. The solution is transferred to a 20-cm. evaporating dish, the flask is rinsed with 50 cc. of water, and the solution and washings are evaporated practically to dryness on a steam bath (Note 2).

The residue is dissolved in 200 cc. of water, transferred to a 1-l. flask, and cooled to 0° in an ice-salt bath. A mixture of 400 cc. of concentrated hydrochloric acid (sp. gr. 1.19) and 200 g. of cracked ice is added slowly until the mixture is acid to Congo red. The temperature of the mixture must not rise above 10° (Note 3). Potassium chloride separates. The mixture is extracted with two 200-cc. portions and four 100-cc.

portions of ether free from alcohol (Note 4) to remove the isopropylmalonic acid. The ether solution (Note 5) is placed in a flask fitted with a reflux condenser, and 160 g. (1 mole) of bromine is added gradually over a period of about two hours at such a rate that the ether boils gently (Note 6). When the bromination is complete, the ether solution is washed with 100 cc. of water to remove the hydrobromic acid, dried over 25 g. of calcium chloride and freed from ether by distillation on the steam bath. The crude isopropylbromomalonic acid is heated in the distilling flask in an oil bath at 125–130° until no more carbon dioxide is evolved. It is then distilled under reduced pressure; the fraction distilling at 140–160°/40 mm. is collected separately and redistilled (Note 7). The yield of product boiling at 148–153°/40 mm. (125–130°/15 mm.) is 100–120 g. (55–66 per cent of the theoretical amount) (Note 8).

2. Notes

1. The isopropylmalonic ester was prepared by the method used for *n*-butylmalonic ester (Org. Syn. **4**, 11). The yield of product boiling at 132–135°/44 mm. was 70–75 per cent of the theoretical amount.

2. Unless the saponification is complete, the final product will contain ethyl α-bromoisovalerate, which will appear in the low-boiling fraction. If all the alcohol is not removed, some esterification will occur on acidification.

3. A rise in temperature favors the loss of carbon dioxide with the formation of isovaleric acid, which will escape bromination.

4. The ether used for extraction is first extracted with one-tenth its volume of saturated calcium chloride solution to remove the alcohol, which would otherwise cause partial esterification of the acid.

5. No special drying is necessary before the bromination, but care should be used in separating the ether and aqueous layers.

6. Usually the bromination starts easily. Sometimes, however, the mixture has to be heated after the first few drops of bromine are added. The mixture may have to be heated to complete the bromination.

7. The product on the first distillation does not have a constant boiling point, as some carbon dioxide is liberated from undecomposed isopropylbromomalonic acid. This cannot be avoided by preliminary heating, even at temperatures much higher than those used.

8. This is a general method for preparing α-bromo acids. By using exactly analogous directions α-bromo-*n*-caproic acid may be obtained in 65–70 per cent yields from *n*-butylmalonic ester; α-bromo-isocaproic acid in 65–70 per cent yields from isobutylmalonic ester; and α-bromo-β-methyl valeric acid in 75–80 per cent yields from sec.-butylmalonic ester.

3. Methods of Preparation

α-Bromoisovaleric acid has been prepared by the action of bromine on isovaleric acid alone,[1] or in the presence of phosphorus;[2] and by the action of heat on isopropylbromomalonic acid.[3]

[1] Ley and Popoff, Ann. **174**, 63 (1874).
[2] Schleicher, Ann. **267**, 115 (1892).
[3] Koenigs and Mylo, Ber. **41**, 4437 (1908).

VII

BROMOMESITYLENE

$$C_6H_3(CH_3)_3 + Br_2 \rightarrow C_6H_2(CH_3)_3Br + HBr$$

Submitted by LEE IRVIN SMITH.
Checked by ROGER ADAMS and H. A. STEARNS.

1. Procedure

IN a 3-l. three-neck flask, provided with a short reflux condenser, a mechanical stirrer and a separatory funnel, is placed a solution of 636 g. (5.3 moles) of mesitylene (Note 1) in 600–700 g. of carbon tetrachloride. The flask is placed in an ice-salt bath and when the reaction mixture is cold (below 10°), a solution of 900 g. (5.6 moles) of bromine in 900 g. of carbon tetrachloride is added to the well-stirred solution. The bromination proceeds very readily, and the hydrogen bromide which is evolved is led off through the condenser and absorbed in water. The addition of the bromine solution requires about three hours, during which time the temperature is maintained at 10–15°.

After the addition of the bromine is complete, the reaction mixture is allowed to stand at room temperature for about one hour. It then has a light-yellow color. The solution is washed with water and then with two 500-cc. portions of 20 per cent sodium hydroxide solution to remove any dissolved hydrobromic acid. The solution is dried over calcium chloride and filtered. The carbon tetrachloride is distilled through a good column until the temperature at the top of the column reaches about 120°.

The residue is added to a solution of 50 g. of sodium in about a liter of 95 per cent alcohol. The solution is boiled under a reflux condenser for about one hour (Note 2) and then allowed to stand overnight. The reaction mixture is diluted with about 6 l. of water and the two layers are separated. The aqueous layer is extracted with three or four 500-cc. portions of carbon

tetrachloride (Note 3), and the extracts are added to the bromomesitylene. This solution is then washed thoroughly with water. The carbon tetrachloride solution is separated, dried over calcium chloride and distilled. After the carbon tetrachloride is removed the bromomesitylene is fractionated carefully under reduced pressure from a modified Claisen flask (Org. Syn. 1, 40). The fraction boiling at 105–107°/16–17 mm. (Note 4) is bromomesitylene. The yield is 840–870 g. (79–82 per cent of the theoretical amount). There is a small low-boiling portion (about 25 g.) and also a small high-boiling residue. The bromomesitylene obtained in this way gives no precipitate on standing twenty-four hours with alcoholic silver nitrate solution. It has a melting point of −1° to +1°.

2. Notes

1. The mesitylene was prepared as described in Org. Syn. **2**, 41 and boiled at 58–59°/15 mm.

2. The treatment with sodium ethylate removed any traces of side chain halogen derivatives. Some care has to be exercised at this point as the solution may foam at the beginning of the heating period.

3. The carbon tetrachloride distilled from the crude bromomesitylene may be used for this purpose. The total volume of solution should be about 2 l.

4. The observed boiling points of bromomesitylene at different pressures were as follows: 132°/62 mm.; 139°/70 mm.; 146°/78 mm.; 157°/100 mm.

3. Methods of Preparation

Bromomesitylene is always made by the bromination of mesitylene in the dark,[1] or in daylight.[2] It has also been made by using mesitylene, ligroin, nitric acid and sulfur bromide.[3]

[1] Schramm, Ber. **19**, 212 (1886).
[2] Fittig and Storer, Ann. **147**, 6 (1868); Smith and MacDougall, J. Am. Chem. Soc. **51**, 3002 (1929).
[3] Ger. pat. 123,746 [Frdl. **6**, 53 (1902)].

VIII

β-CHLOROPROPIONALDEHYDE ACETAL

$$CH_2{=}CHCHO + 2C_2H_5OH + HCl \rightarrow ClCH_2CH_2CH(OC_2H_5)_2 + H_2O$$

Submitted by E. J. WITZEMANN, WM. LLOYD EVANS, HENRY HASS, and E. F. SCHROEDER.
Checked by FRANK C. WHITMORE and HARRY T. NEHER.

1. Procedure

IN a 3-l. round-bottom flask, fitted with a mechanical stirrer and an inlet tube, is placed 200 g. of absolute alcohol (Note 1). The flask is surrounded by an ice-salt bath, and the alcohol is saturated with dry hydrogen chloride (Org. Syn. **2**, 30) at 0°. The stem of a 200-cc. separatory funnel is fitted to a one-hole stopper inside a large short-stem funnel (Fig. 1). The space between the funnels is filled with finely cracked ice and water. In the separatory funnel is placed 112 g. (2 moles) of cold acrolein (Org. Syn. **6**, 1) (Note 2).

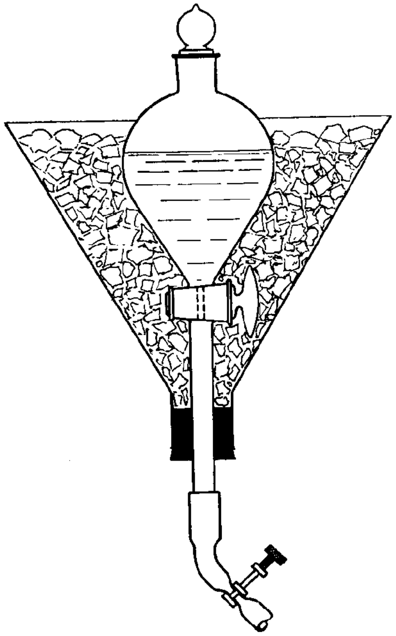


FIG. 1.

When the alcohol is saturated with hydrogen

chloride, the generator is disconnected and the stem of the separatory funnel is connected to the inlet tube by a rubber tube provided with a screw clamp for adjusting the flow. The acrolein is added, with stirring, to the alcoholic hydrogen chloride solution at about 0°. The addition should require from one to two hours. After two layers have formed the lower layer is separated and treated gradually with powdered sodium bicarbonate until all acid is neutralized (Note 3). The mixture is filtered. The filtrate is washed with two 50-cc. portions of ice water and dried over 10 g. of potassium carbonate for five to ten hours. It is then filtered and distilled under reduced pressure. The yield of product boiling at 58-62°/8 mm. is 112 g. (34 per cent of the theoretical amount).

2. Notes

1. At least 99.5 per cent alcohol should be used (Org. Syn. **5**, 56).
2. If the acrolein is not kept cold, the vapors become unbearable. The stopper of the separatory funnel should be provided with a fine glass capillary.
3. All acid must be removed before washing the product with water, because dilute acid hydrolyzes the acetal very readily.

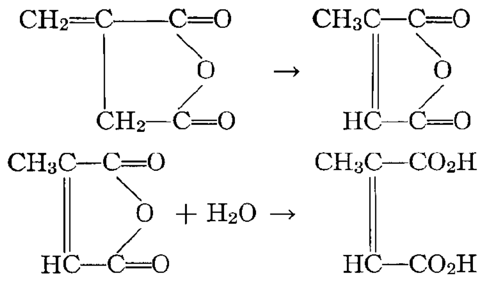
3. Methods of Preparation

β-Chloropropionaldehyde acetal has been prepared by the action of acrolein on alcoholic hydrogen chloride alone,[1] or in the presence of calcium chloride.[2]

[1] Alsberg, Jahresber. **1864**, 495; Wohl, Ber. **31**, 1797 (1898); Wohl and Emmerich, Ber. **33**, 2761 (1900); Brabant, Z. physiol. Chem. **86**, 208 (1913); Witzemann, J. Am. Chem. Soc. **36**, 1909 (1914); Spoehr and Young, Carnegie Inst. Washington Yearbook, **25**, 176 (1925–1926); Expt. Sta. Record, **57**, 817 (1927) [C. A. **22**, 2368 (1927)].
[2] Crawford and Kenyon, J. Chem. Soc. **1927**, 399.

IX

CITRACONIC ANHYDRIDE AND CITRACONIC ACID



Submitted by R. L. Shriner, S. G. Ford, and L. J. Roll.
Checked by C. R. Noller.

1. Procedure

A. *Citraconic Anhydride*: Two hundred and fifty grams of itaconic anhydride (Note 1) is distilled rapidly at atmospheric pressure in a 500-cc. modified Claisen flask with a 15-cm. (6-in.) fractionating column (Note 2). The receivers for the distillate must be changed without interrupting the distillation. The distillate passing over below 200° consists of water and other decomposition products. The fraction which distils at 200–215° consists of citraconic anhydride and is collected separately. The yield is 170–180 g. (68–72 per cent of the theoretical amount) of a product melting at 5.5–6°. On redistillation under reduced pressure there is obtained a yield of 155–165 g. (62–66 per cent of the theoretical amount based on the itaconic anhydride used) of a product which boils at 105–110°/22 mm. and melts at 7–8° (Note 3).

B. *Citraconic Acid*: To 22.4 g. (0.2 mole) of pure citraconic anhydride in a 100-cc. beaker is added from a pipette exactly

4 cc. (0.22 mole) of distilled water. The mixture is stirred on a hot plate until a homogeneous solution is formed, then covered with a watch glass and allowed to stand for forty-eight hours. At the end of this time the mixture has solidified completely. The yield is 26 g. of a product melting at 87–89°. For further purification it is finely ground in a mortar, washed with 50 cc. of cold benzene, dried in the air, and then dried for twenty-four hours in a vacuum desiccator over phosphorus pentoxide. The yield is 24.4 g. (94 per cent of the theoretical amount) of a product which melts at 92–93°.

2. Notes

1. The crude itaconic anhydride obtained as described on page 70 was used. Itaconic acid may be substituted for the anhydride.

2. The success of the preparation depends upon a rapid distillation and changing the receivers without interrupting the distillation. The best yields are obtained when the heating period is of short duration.

3. The crude citraconic anhydride contains a small amount of water, acetone and citraconic acid. Vacuum distillation allows the removal of these impurities without materially decreasing the yield.

3. Methods of Preparation

Citraconic anhydride has been prepared by the distillation of citraconic acid and of citric acid.[1]

Citraconic acid has been obtained by distillation of citric acid,[2] of lactic acid,[3] and of hydroxypyrotartaric acid;[4] and by treating citric acid with hydriodic acid.[5]

[1] Anschutz, Ber. **14**, 2788 (1881).
[2] Crasso, Ann. **34**, 68 (1840); Kekulé, "Lehrbuch der Organischen Chemie," **2**, 317 (1866); Wilm, Ann. **141**, 28 (1867).
[3] Engelhardt, Ann. **70**, 243, 246 (1849).
[4] Demarçay, Ber. **9**, 963 (1876).
[5] Kämmerer, Ann. **139**, 269 (1866).

X

CYANOGEN BROMIDE

$$NaCN + Br_2 \rightarrow BrCN + NaBr$$

Submitted by W. W. Hartman and E. E. Dreger.
Checked by Roger Adams and I. L. Ozanne.

1. Procedure

A 2-l. round-bottom flask, surrounded by an ice-water bath and provided with a stirrer, a separatory funnel and an outlet tube, is set up in a good hood. To the flask are added 500 g. (3.1 moles) of bromine and 50 cc. of water (Note 1). To the stirred mixture is added gradually a solution of 170 g. of sodium cyanide (3.4 moles) in 1200 cc. of warm water. The temperature of the reaction mixture is kept below 30°. When the reaction is complete (about two hours or less) the cyanogen bromide is distilled from a steam bath, using a 500-cc. flask (Note 2) as a receiver. The distillate is warmed with about 100 g. of anhydrous calcium chloride, filtered and again distilled, preferably from one distilling flask directly into another, the neck of which is fitted to the side-arm of the first. The cyanogen bromide boils at 60–62°. It is melted in the receiver (Note 3) (Hood) and poured into a warm tared bottle. The yield of white crystalline solid (Note 4) melting at 49–51° is 239–280 g. (73–85 per cent of the theoretical amount).

2. Notes

1. Water is used to decrease the volatilization of the bromine.
2. It is desirable to have the receiving flask close to the distilling flask because there is a tendency for the cyanogen bromide to clog a tube which is too small in diameter or too long.

3. Because of the toxic nature of the product it is best to wear a gas mask while transferring the molten product.
4. Cyanogen bromide does not keep well and may at times even become explosively unstable on standing. It is preferable to prepare it just before using.

3. Methods of Preparation

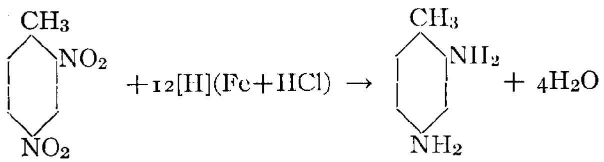
Cyanogen bromide has been prepared from an aqueous solution of potassium cyanide and bromine at 0°,[1] and by the action of bromine on moist mercuric cyanide.[2]

[1] Langlois, Ann. chim. phys. (3), **61**, 482 (1861); Scholl, Ber. **29**, 1823 (1896); Baum, Ber. **41**, 523 (1908).

[2] Serullas, Ann. chim. phys. (2), **34**, 100 (1827).

XI

2,4-DIAMINOTOLUENE



Submitted by S. A. Mahood and P. V. L. Schaffner.
Checked by Roger Adams and P. R. Shildneck.

1. Procedure

In a 500-cc. three-neck flask, fitted with a reflux condenser and a mechanical stirrer (Note 1), is placed 45.5 g. (0.25 mole) of 2,4-dinitrotoluene (Note 2), 85 g. (1.5 moles) of iron (Note 3), and 100 cc. of 50 per cent (by weight) ethyl alcohol (Note 4). The mixture is heated to boiling on a water bath, the stirrer is started (Note 5) and a solution of 5.2 cc. (0.06 mole) of concentrated hydrochloric acid in 25 cc. of 50 per cent (by weight) ethyl alcohol is added slowly (Note 6). The mixture is refluxed for two hours after addition of the acid is complete. At the end of this time the apparatus is disconnected and the hot mixture is made just alkaline to litmus by the addition of the calculated amount of 15 per cent alcoholic potassium hydroxide solution (Note 7). Without allowing the mixture to cool, the iron is removed by filtration and the reaction flask is rinsed with two 50-cc. portions of 95 per cent ethyl alcohol; the same alcohol is used to wash the iron residue. To the filtrate is added 84 cc. of 6 N sulfuric acid; the normal sulfate of 2,4-diaminotoluene precipitates. The mixture is cooled to 25° and filtered by suction. The product is washed with two 25-cc. portions of 95 per

cent ethyl alcohol, dried in the air for two hours (Note 8) and then dried to constant weight at 110°. The yield is 49 g. (89 per cent of the theoretical amount) of a product which melts with decomposition at 249–251° (Note 9).

A solution of 20 g. of 2,4-diaminotoluene sulfate in 200 cc. of water at 60° is cooled to 40° (Note 10), and made alkaline to litmus with saturated sodium hydroxide solution (Note 11). To this solution is added 15 g. of the sulfate and this is dissolved by raising the temperature of the mixture to 55°. The solution is cooled to 40° and made slightly alkaline to litmus with saturated sodium hydroxide solution. The mixture is then cooled to 30° and filtered by suction. The remainder of the diaminotoluene sulfate (14 g.) is then dissolved in the filtrate by heating the mixture to 55°. The solution is cooled to 40° and again made alkaline to litmus with saturated sodium hydroxide solution. The mixture is cooled to 25° and the diaminotoluene crystals are collected on a Büchner funnel. The entire product is dried to constant weight in a desiccator over calcium chloride. The yield is 26.5 g. (95 per cent of the theoretical amount based on the diaminotoluene sulfate used) of a product melting at 97–98.5°.

The crude diaminotoluene (Note 12) is dissolved in eight times its weight of benzene (212 g.) at 70°, and the solution is filtered quickly through a hot Büchner funnel (Note 13) with moderate suction (Note 14). The filtrate is cooled to 25° and the mother liquor is decanted from the brown crystals. The mother liquor is concentrated to a volume of 25 cc. by distillation under atmospheric pressure, and then cooled to 25°. The mother liquor is decanted from the diaminotoluene and the entire product is dried in the air. The yield is 22.5 g. (81 per cent of the theoretical amount based on the diaminotoluene sulfate used; 74 per cent based on the dinitrotoluene used) of a product which melts at 98°.

2. Notes

1. The mechanical stirrer should extend well to the bottom of the flask in order to prevent caking of the iron during the reduction.

2. The 2,4-dinitrotoluene used must be free from oil and have the correct melting point of 71°.

3. The iron used may be either iron powder or iron filings, but it should pass a 100-mesh sieve in order to give invariable results. If iron particles of larger size are used, the reduction may be incomplete although complete reduction was obtained with a sample of iron powder contaminated with filings.

4. The concentration of the alcoholic solution is important. Incomplete reduction was obtained with 95 per cent alcohol, as well as with methylated spirit, as suggested by West.[1] Complete reduction may be obtained in aqueous solution, but the product is difficult to isolate and is not always pure.

5. The stirrer should be run at such a speed that the iron particles do not settle or the iron will cake during the reduction. A speed of about 750 r.p.m. is satisfactory.

6. The reaction between the iron and hydrochloric acid is very vigorous, especially in the case of iron powder, and the hydrochloric acid must be added very slowly at first. About one drop every ten seconds for the first ten minutes is satisfactory and this may be increased to one drop every four seconds after this length of time has elapsed. The addition of the hydrochloric acid should require about thirty minutes.

7. The exact amount of alcoholic potassium hydroxide is determined previously by titration of a separate sample of 5.2 cc. of concentrated hydrochloric acid with the alcoholic potassium hydroxide.

8. Most of the alcohol and any aldehyde must be removed by evaporation at room temperature since heating the wet product at once to 110° always causes the formation of orange-colored impurities.

[1] West, J. Chem. Soc. **127**, 494 (1925).

9. The same percentage yields of the sulfate were obtained using six times the amounts of materials.

10. The solution is cooled before addition of the alkali, as this is accompanied by a rise in temperature.

11. Saturated sodium hydroxide solution is used rather than more dilute solutions since dilution of the diaminotoluene solution is to be avoided as much as possible.

12. The diaminotoluene obtained by neutralizing the sulfate contains varying amounts of sodium sulfate and possibly some diaminotoluene sulfate, both of which are insoluble in benzene.

13. A hot Büchner funnel (70° or above) is used to prevent crystallization of the diaminotoluene in the funnel.

14. Moderate suction is used to prevent boiling of the benzene since this causes crystallization of the diaminotoluene in the funnel.

15. In an attempt to prepare a pure white product, the dry recrystallized material was distilled rapidly at atmospheric pressure using a short air condenser. A yellow product distilling at 292° was obtained. On distilling the recrystallized material at 148–150°/8 mm., a white product was obtained.

3. Methods of Preparation

2,4-Diaminotoluene has been prepared from 2,4-dinitrotoluene by reduction with iron and acetic acid,[2] and by electrolytic reduction;[3] from 4-nitro-*o*-toluidine by reduction with tin and hydrochloric acid;[4] and from 2,4-dinitrobenzoyl chloride with tin and hydrochloric acid.[5]

[2] Hofmann, Jahresber. **1861**, 512.

[3] Hofer and Jakob, Ber. **41**, 3192 (1908).

[4] Nölting and Collin, Ber. **17**, 268 (1884).

[5] Krasusky, J. Russ. Chem. Soc. **27**, 337 (1896).

XII

ETHYL ETHYLENETETRACARBOXYLATE

$$2CHBr(CO_2C_2H_5)_2 + Na_2CO_3 \rightarrow$$
$$2NaBr + H_2O + CO_2 + (C_2H_5O_2C)_2C{=}C(CO_2C_2H_5)_2$$

Submitted by B. B. Corson and W. L. Benson.
Checked by C. S. Marvel and H. E. Munro.

1. Procedure

A mixture of 200 g. (1.9 moles) of anhydrous sodium carbonate (Note 1) and 300 g. (1.25 moles) of ethyl bromomalonate (Org. Syn. 7, 34) is heated for three hours in a 1-l. flask (Note 2) immersed in an oil bath at 150–160° (Note 3). After the heating period, 300 cc. of xylene (Note 4) is added while the contents of the flask are still hot (Note 5). The solid is broken up carefully with a rod and the mixture is transferred to a 2-l. beaker. The reaction flask is then rinsed with a mixture of 100 cc. of xylene and 100 cc. of water. This washing is poured into the 2-l. beaker and an additional 600 cc. of water is added. The solid readily dissolves upon stirring. The liquid mixture is transferred to a separatory funnel, shaken well, and allowed to settle (Note 6). The lower aqueous layer is discarded (Note 7). The xylene layer is transferred to a 1-l. distilling flask and distilled until the temperature of the liquid itself is 170°. The liquid residue is then transferred to a 500-cc. Claisen flask and distilled under reduced pressure. The forerun up to 170°/15 mm. is discarded. The product is collected at 170–230°/15 mm. (Notes 8 and 9). The distillate solidifies within about fifteen minutes. The yield is 150–160 g. (75–80 per cent of the theoretical amount).

The crude product is dissolved in 75 cc. of 95 per cent alcohol at a temperature of 40°, which is sufficient to insure complete solution. The alcoholic solution is cooled to 12° (Notes 10 and 11) and filtered. The yield of air-dried, colorless product melting at 52.5–53.5° is 95–110 g. (47–55 per cent of the theoretical amount). By evaporation of the alcohol, distillation of the residue under reduced pressure, and recrystallization of the solidified distillate, the yield may be increased to 110–115 g. (55–57 per cent of the theoretical amount).

2. Notes

1. The sodium carbonate should be fine enough to pass through a 100-mesh sieve.

2. The mixture is heated in an open flask. Due to the high boiling points of ethyl bromomalonate and ethyl ethylenetetracarboxylate, there is but little loss by volatilization. On the other hand, the yield is lowered by the use of a condenser, presumably because the water formed by the reaction is kept in the reaction mixture with resultant hydrolysis of one or both of the esters.

3. The flask is placed in the cold bath. The three hours are counted from the time that the temperature of the bath reaches 150°.

4. Toluene or benzene can be substituted for xylene, but xylene is preferable because of its higher boiling point.

5. If the mixture is allowed to cool, it solidifies and renders removal difficult.

6. A good separation is obtained in ten minutes.

7. Experiment has shown that the amount of product in the aqueous layer is negligible.

8. Ethyl ethylenetetracarboxylate boils at 197°/8 mm.; 203°/13 mm.; 210°/22 mm.; 221°/33 mm.; 234°/48 mm.

9. There is very little residue left in the flask. Distillation should be stopped as soon as dark-yellow drops of distillate begin to come over.

10. The crystallization mixture is a thick slush with low

heat conductivity, hence a rather long cooling period is necessary to lower the temperature to 12°. A thermometer should be used because it is important that the mixture be cooled to 12°, since the solubility curve begins to rise above 12°. There is no advantage in cooling below 12°.

11. The solubility of ethyl ethylenetetracarboxylate in 100 cc. of 95 per cent ethyl alcohol is as follows:

2.0 g. at 0°	16.0 g. at 30°
2.5 g. at 11°	19.0 g. at 31°
4.0 g. at 16°	28.0 g. at 33°
8.0 g. at 23°	35.0 g. at 34°
9.7 g. at 26°	61.0 g. at 36.5°

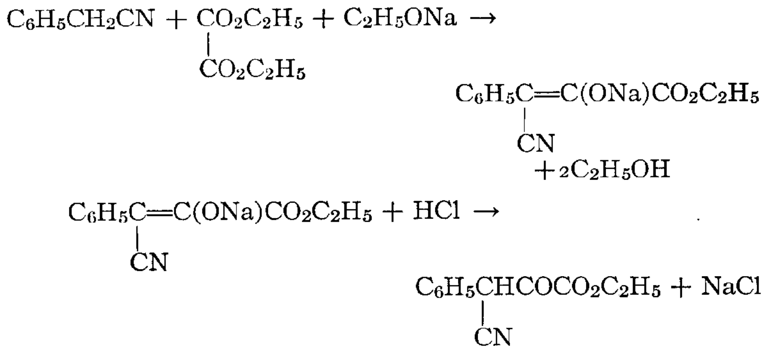
3. Methods of Preparation

Ethyl ethylenetetracarboxylate has been prepared from monochloro- and monobromomalonic ester through removal of halogen acid with sodium,[1] sodium ethylate,[2] potassium acetate,[3] potassium carbonate,[4] sodium urethane,[5] sodium formanilide and sodium acetanilide.[6] It has also been prepared by treating the disodium derivative of ethyl ethane-1,1,2,2-tetracarboxylate with bromine,[7] or iodine;[8] by treating dibromomalonic ester with sodium,[9] or sodium ethylate;[10] and by treating the disodium derivative of malonic ester with iodine.[11]

[1] Conrad and Guthzeit, Ber. **16**, 2631 (1883).
[2] Conrad and Guthzeit, Ann. **214**, 76 (1882).
[3] Conrad and Brückner, Ber. **24**, 2998 (1891).
[4] Blank and Samson, Ber. **32**, 860 (1899).
[5] Diels and Heintzel, Ber. **38**, 303 (1905).
[6] Paal and Otten, Ber. **23**, 2591 (1890).
[7] Kötz and Stalmann, J. prakt. Chem. (2) **68**, 163 (1903)
[8] Bischoff and Hausdörfer, Ann. **239**, 130 (1887).
[9] Conrad and Brückner, Ber. **24**, 3004 (1891).
[10] Curtiss, Am. Chem. J. **19**, 699 (1897).
[11] Bischoff and Rach, Ber. **17**, 2781 (1884).

XIII

ETHYL PHENYLCYANOPYRUVATE



Submitted by Roger Adams and H. O. Calvery.
Checked by J. B. Conant and Doris Blumenthal.

1. Procedure

In a 3-l. round-bottom flask, fitted with a reflux condenser, is placed 650 cc. of absolute alcohol (Org. Syn. **5**, 56) and to it 46 g. (2 moles) of sodium is added as rapidly as possible without loss of material through the condenser. If all the sodium does not dissolve, heat is applied. To the hot sodium ethylate solution 312 g. (2.1 moles) of ethyl oxalate (Org. Syn. **2**, 23; **5**, 59) is added as rapidly as possible. Then, immediately, 234 g. (2 moles) of benzyl cyanide (Org. Syn. **2**, 9) is added. The reaction mixture is allowed to stand overnight. The solution is transferred to a 3-l. beaker and treated with 250-300 cc. of water (Note 1). It is then warmed to 35°, and made strongly acid to litmus with concentrated hydrochloric acid. Mechanical stirring is used during the acidification. On cooling to ordinary

temperatures the ester crystallizes. The yield is 360–385 g. of lemon-yellow crystals melting at 126–128°. On recrystallization from 60 per cent alcohol, the ester melts at 130°. The final yield is 300–325 g. (69–75 per cent of the theoretical amount).

2. Notes

1. This amount of water dilutes the alcohol so that the ester crystallizes well. If more water is used an oily product separates and then solidifies.

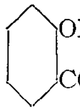
3. Methods of Preparation

The only method of preparation mentioned in the literature is that given above.[1]

[1] Erlenmeyer, Ann. **271**, 173 (1893).

XIV

ETHYL PIMELATE



OH

$CO_2H + 4[H] + H_2O \rightarrow HO_2C(CH_2)_5CO_2H$

$$HO_2C(CH_2)_5CO_2H + 2C_2H_5OH \rightarrow C_2H_5O_2C(CH_2)_5CO_2C_2H_5 + 2H_2O$$

Submitted by Adolf Müller and Erich Rölz.
Checked by W. H. Carothers and W. L. McEwen.

1. Procedure

In a 5-l. two-neck flask, fitted with a 1-l. separatory funnel and a reflux condenser, and surrounded by an oil bath, is placed 250 cc. of freshly distilled isoamyl alcohol (b.p. 128–135°). While the alcohol is being heated rapidly to boiling, 120 g. of sodium, cut in large pieces is added. As soon as the alcohol boils, a solution of 50 g. (0.36 mole) of salicylic acid in 1 l. of isoamyl alcohol is added. At first the solution is introduced in a rapid stream of drops, but after a few minutes the rate is regulated so that the addition is complete in about one hour. The temperature of the reaction mixture is adjusted so that the liquid returns from the condenser at the rate of about one drop per second. This rate of boiling is maintained throughout this part of the preparation. Two hours and forty-five minutes from the beginning of the addition of the salicylic acid solution, 125 cc. of isoamyl alcohol is added rapidly. Forty-five minutes later, another 125-cc. portion of isoamyl alcohol is added rapidly. All the sodium does not dissolve until about five hours from the beginning of the preparation (Note 1).

The solution is cooled to 60–70°, then washed with two 1-l. portions of warm water (50–60°) (Note 2). The aqueous extracts are evaporated on a steam bath until there is formed a thick, crystalline magma which has only a faint odor of isoamyl alcohol (Note 3). The magma is dissolved in 300 cc. of water, and 400 cc. of concentrated hydrochloric acid is added. The mixture is cooled to room temperature, filtered (Note 4) and 85 cc. more of concentrated hydrochloric acid is added to the filtrate. The acid mixture is extracted with three 200-cc. portions of ether (Note 5), and the ether is removed by distillation. Upon cooling the residue in an ice bath, crystals separate, and after thorough cooling these are collected on a Büchner funnel and then pressed on a porous plate. The filtrate, after adding a few pieces of porous plate, is allowed to stand overnight in a vacuum desiccator over concentrated sulfuric acid. The crystals which separate are collected on a filter, pressed on porous plate and added to the rest of the product. The total weight is 30–35 g. (Note 6).

The crude material, which is a mixture of pimelic acid and unchanged salicylic acid, is esterified by boiling for four hours with 260 cc. of absolute ethyl alcohol and 3 cc. of concentrated sulfuric acid. Two-thirds of the alcohol is then removed by distillation. To the residue, 300 cc. of water and 200 cc. of ether are added, the mixture is shaken and the aqueous layer is removed. The ether solution is washed with two 100-cc. portions of 2 N sodium hydroxide solution to remove the ethyl salicylate (Note 7) and then with water until the disappearance of an alkaline reaction. The ether is evaporated and the residue is distilled under reduced pressure. The ethyl pimelate boils at 153–156°/24 mm.; 148–152°/22 mm. The yield is 27–30 g. (35–38 per cent of the theoretical amount based upon the salicylic acid used).

2. Notes

1. At this time there may be a very small quantity of sodium remaining undissolved. If care is used in adding the water, no trouble with fire or explosion occurs.

2. Unless the solutions are kept at approximately the temperatures indicated there is difficulty with the separation. Even with warm solutions the separation is often very slow.

3. A large proportion of the isoamyl alcohol used may be recovered for use in subsequent preparations. The moist alcohol from the water extractions is directly distilled and a fraction boiling at 128–135° is collected. The alcohol layer in the fore-run is separated and it may either be added to the alcohol from the following run, or subjected to distillation separately and a fraction of the same boiling range collected as before. Alcohol thus recovered is perfectly satisfactory for the preparation of pimelic acid.

4. A satisfactory ether extraction can only be obtained by first removing the brown sludge produced by partial acidification. If all the acid is added at once, ether extraction of the entire precipitate is very tedious because of the slow separation of the aqueous and ether layers.

5. A continuous ether extraction in an apparatus such as is described in Org. Syn. 3, 88 may be used at this point with considerable advantage.

6. The crystals of pimelic and salicylic acids may be dried overnight in a vacuum desiccator and then on filter paper if porous plate is not available.

7. If the washing with sodium hydroxide is not carefully done some loss of product due to hydrolysis may occur.

3. Methods of Preparation

Pimelic acid has been prepared as a by-product of the reaction between trimethylene bromide and sodium cyanoacetic ester;[1] by the action of carbon dioxide upon pentamethylene-

[1] Carpenter and Perkin, J. Chem. Soc. **75**, 933 (1899).

1,5-dimagnesium bromide;[2] by hydrolysis of pentamethylene cyanide;[3] and by the action of sodium amylate upon salicylic acid, guaiacol carboxylic acid,[4] and anthranilic acid.[5]

The ethyl ester has always been prepared by action of sulfuric acid and absolute alcohol upon the acid.[6]

The above directions were recently described in the literature.[6]

[2] Grignard and Vignon, Compt. rend. **144**, 1359 (1907).

[3] Hamonet, Compt. rend. **139**, 60 (1904); Bull. soc. chim. (3) **33**, 532 (1905); v. Braun, Ber. **37**, 3591 (1904).

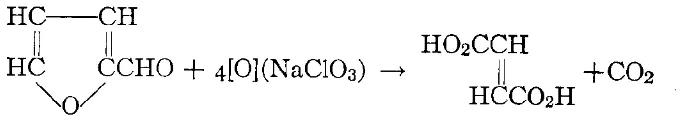
[4] Einhorn and Lumsden, Ann. **286**, 259, 266 (1895); Walker and Lumsden, J. Chem. Soc. **79**, 1198 (1901).

[5] Einhorn and Meyenberg, Ber. **27**, 2467 (1894).

[6] Müller and Rölz, Monatsh. **48**, 734 (1927).

XV

FUMARIC ACID



Submitted by Nicholas A. Milas.
Checked by Roger Adams and K. L. Amstutz.

1. Procedure

In a 5-l. flat-bottom flask, equipped with a condenser (Note 1), a separatory funnel and a mechanical stirrer (Note 2), are placed 450 g. (2.24 moles) of sodium chlorate, 2 g. of vanadium pentoxide (Note 3) and 1 l. of water. The mixture is heated (Note 4) to 70–75° by supporting the flask 10 cm. above an electric hot plate. To the well-stirred solution is then added 200 g. (2.06 moles) of furfural (Note 5) over a period of seventy to eighty minutes. After the addition of furfural is complete, the mixture is heated at 70–75°, with stirring, for ten to eleven hours, and then allowed to stand at room temperature overnight. The mixture is filtered by suction, and the crude fumaric acid is dried in the air. The yield is 155–170 g. (65–72 per cent of the theoretical amount) (Note 6).

More fumaric acid may be obtained from the filtrate by heating it on the water bath with 50 cc. of concentrated hydrochloric acid; the solution usually turns blue at the end of the reaction. The solution is concentrated to about 700 cc. and then cooled with running water. The fumaric acid which separates is collected on a filter and dried in the air. The yield is 10–15 g. of a product which melts at 282–284° in a sealed tube.

The crude product is purified by recrystallization from about 1250 cc. of 1 N hydrochloric acid. This gives 100–110 g. of pure fumaric acid melting at 282–284° in a sealed tube. An additional amount of fumaric acid may be obtained by concentrating the filtrate to a small volume on a water bath.

The total yield of pure fumaric acid is 120–138 g. (50–58 per cent of the theoretical amount).

2. Notes

1. The condenser should be 80–90 cm. (32–36 in.) long and fitted with a wide inner tube.

2. The yields were lower when mechanical stirring was not used.

3. The catalyst is prepared by suspending 20 g. of c.p. ammonium metavanadate in 200 cc. of water and adding slowly 30 cc. of concentrated hydrochloric acid (sp. gr. 1.19). The reddish-brown semi-colloidal precipitate is washed several times with water by decantation and finally suspended in 300 cc. of water and allowed to stand at room temperature for three days. This treatment makes the precipitate granular and easy to filter. The precipitate is collected on a filter using a pump and washed several times with water to free it from hydrochloric acid. It is then dried at 120° for twelve hours, finely powdered and again dried for twelve hours at 120°.

4. To observe the temperature, a thermometer may be suspended in the flask through the inner tube of the condenser. The mixture may be heated first to 70–75° over a free flame.

5. The furfural used was the technical grade furnished by the Miner Laboratories, Chicago. According to these laboratories the furfural was "about 99 per cent pure." The crude furfural obtained as described in Org. Syn. 1, 49 may be used.

The reaction does not seem to start immediately upon the addition of the first few cubic centimeters of furfural. It is best to add first 5–10 cc. of furfural and allow the reaction to start. When the vigorous reaction commences, the temperature rises to about 105° and remains there until the reaction

becomes moderate. The yield of fumaric acid seems to depend somewhat upon the rapidity of the first stage of the reaction. It is therefore necessary to regulate the addition of furfural so that a vigorous reaction is maintained.

6. The crude fumaric acid is from 74–78 per cent pure as found by titration with standard alkali. The only impurity present besides inorganic salts consists of small quantities of sodium hydrogen maleate which is decomposed by the hydrochloric acid during the purification process.

3. Methods of Preparation

Fumaric acid has been prepared from bromosuccinic acid by heating with water,[1] or dilute hydrobromic acid,[2] and by heating the acid above its melting point.[3] It has also been prepared by heating malic acid,[4] by transmutation of maleic acid;[5] and by the reduction of tartaric acid with phosphorus and iodine.[6] The procedure described is the most satisfactory for laboratory use, and is a slight modification of one recently described in the literature.[7]

[1] Volhard, Ann. **268**, 256 (1892); Müller and Suckert, Ber. **37**, 2598 (1904).

[2] Fittig, Ann. **188**, 90 (1877).

[3] Kekulé, Ann. **130**, 22 (1864); Volhard, Ann. **242**, 158 (1887).

[4] Lassaigne, Ann. chim. phys. (2) **11**, 93 (1819); Pelouze, Ann. **11**, 265 (1834); Wislicenus, Ann. **246**, 91 (1888); Michael, J. prakt. Chem. (2) **46**, 231 (1892); Jungfleisch, Bull. soc. chim. (2) **30**, 147 (1878).

[5] Wislicenus, Ber. 29, 1080 (abstracts) (1896); Ciamician and Silber, Ber. **36**, 4267 (1903); Skraup, Monatsh. **12**, 107 (1892); Weiss and Downs, J. Am. Chem. Soc. **44**, 1119 (1922); Terry and Eichelberger, J. Am. Chem. Soc. **47**, 1410 (1925).

[6] Ger. pat. 254,420 [Frdl. **11**, 99 (1912)]; Org. Chem. Reagents **II**, University of Illinois Bulletin, Vol. XVIII, No. 6, page 35 (1920).

[7] Milas, J. Am. Chem. Soc. **49**, 2007 (1927).

XVI

dl-GLYCERIC ALDEHYDE

$$HOCH_2CHOHCH(OC_2H_5)_2 + H_2O(H_2SO_4) \rightarrow HOCH_2CHOHCHO + 2C_2H_5OH$$

Submitted by E. J. Witzemann, Wm. Lloyd Evans, Henry Haas, and E. F. Schroeder.
Checked by Frank C. Whitmore and Harry T. Neher.

1. Procedure

A mixture of 50 g. (0.3 mole) of *dl*-glyceric aldehyde acetal (p. 52) and 500 cc. of 0.1 N sulfuric acid is allowed to stand for one week at about 20° (Note 1). The mixture is then treated with 30 cc. of glacial acetic acid and neutralized carefully with barium hydroxide solution (Note 2). The mixture is stirred with 5 g. of decolorizing carbon and filtered. The filtrate is evaporated at 10 mm. pressure (Note 3). When no more water can be removed, the residue is treated with an equal volume of absolute alcohol to hasten crystallization. The crystals are collected on a filter and dried in a vacuum desiccator over soda-lime and calcium chloride. The yield of product melting at 137–139° is 22 g. (80 per cent of the theoretical amount) (Note 4).

2. Notes

1. During this part of the preparation, including the evaporation, the temperature should be kept below 30°. If this precaution is rigidly observed, the glyceric aldehyde crystallizes readily.

2. Samples of the filtered solution should give only a very

slight opalescence when tested with barium hydroxide and with sulfuric acid.

3. The use of 10 mm. instead of 20 mm. pressure for the evaporation improves the quality of the glyceric aldehyde, making the difference between a syrup which may or may not crystallize and a product which even crystallizes from the concentrated solution.

4. The yield based on the acrolein used (p. 26) is about 11 per cent of the theoretical amount.

3. Methods of Preparation

dl-Glyceric aldehyde has been obtained by the oxidation of glycerol with nitric acid,[1] with bromine and sodium carbonate,[2] and with hydrogen peroxide in the presence of ferrous salts;[3] by the action of ultraviolet light on glycerol in neutral solution;[4] by the action of sunlight on glycerol in the presence of uranium sulfate;[5] by electrolysis of *dl*-erythronic acid;[6] by the hydrolysis of *dl*-glyceric aldehyde acetal;[7] and by the oxidation of acrolein.[8]

[1] Kiliani, Ber. **54**, 467 (1921); Fischer and Tafel, Ber. **20**, 3385 (1887).

[2] Fischer and Tafel, Ber. **20**, 3385 (1887).

[3] Fenton and Jackson, Chem. News, **78**, 187 (1898); J. Chem. Soc. **75**, 5 (1899); Witzemann, J. Am. Chem. Soc. **36**, 2227 (1914).

[4] Bierry, Henri and Ranc, Compt. rend. **152**, 535 (1911).

[5] Neuberg, Biochem. Z. **13**, 307 (1908).

[6] Neuberg, Scott, and Lachmann, Biochem. Z. **24**, 157 (1910).

[7] Wohl, Ber. **31**, 1800, 2395 (1898); Wohl and Neuberg, Ber. **33**, 3100 (1900); Evans and Hass, J. Am. Chem. Soc. **48**, 2706 (1926); Witzemann, *ibid.* **36**, 1913 (1914); Spoehr and Young, Carnegie Inst. Washington Yearbook, **25**, 177 (1925-1926); Exp. Sta. Record, **57**, 817 (1927) [C. A. **22**, 2368 (1928)].

[8] Neuberg, Biochem. Z. **221**, 492 (1930).

XVII

dl-GLYCERIC ALDEHYDE ACETAL

$$CH_2{=}CHCH(OC_2H_5)_2 + H_2O + [O](KMnO_4) \rightarrow HOCH_2CHOHCH(OC_2H_5)_2$$

Submitted by E. J. WITZEMANN, WM. LLOYD EVANS, HENRY HASS, and E. F. SCHROEDER.
Checked by FRANK C. WHITMORE and HARRY T. NEHER.

1. Procedure

IN a 3-l. open flask, equipped with a mechanical stirrer and a thermometer, and cooled in an ice bath, is placed a suspension of 65 g. (0.5 mole) of acrolein acetal (p. 1) in 600 cc. of water. The suspension is cooled to 5° (Note 1) and a solution of 80 g. (0.5 mole) of potassium permanganate in 1500 cc. of water is added, with stirring, at the rate of about 25 cc. per minute. The temperature is kept as near 5° as possible during the addition. Soon after the stirring is stopped, the mixture sets to a gel (Note 2). After standing for two hours, the mixture is heated for one hour on the steam bath and then filtered by suction on a large (30-cm.) Büchner funnel. The residual manganese dioxide is pressed thoroughly and washed with 150 cc. of cold water. The filtrate (about 2300 cc.) is kept cool and treated with 1200 g. of freshly dehydrated commercial potassium carbonate. The layers are separated and the water layer is extracted with four 100-cc. portions of ether. The ether extracts are added to the crude acetal layer and the mixture, which may consist of two layers (Note 3), is dried over 10 g. of potassium carbonate. After removal of the ether, the residue is distilled under reduced pressure. The yield of product boiling at 120–121°/8 mm. is 55 g. (67 per cent of the theoretical amount).

2. Notes

1. The oxidation is very sensitive to changes in temperature. The best results are obtained at 5°; a slight variation causes a marked decrease in the yield.

2. If the mixture does not set to a gel, the yield is likely to be poor. This is usually due to poor temperature control.

3. Sometimes two layers appear at first, but these disappear when the potassium carbonate is added.

3. Methods of Preparation

dl-Glyceric aldehyde acetal has been prepared by heating hydroxychloropropionaldehyde acetal with potassium carbonate solution;[1] by treating glyceric aldehyde with alcoholic hydrogen chloride;[2] and by oxidation of acrolein acetal with potassium permanganate.[3]

[1] Wohl, Ber. **31**, 1799 (1898).

[2] Wohl and Neuberg, Ber. **33**, 3103 (1900); Witzemann, J. Am. Chem. Soc. **36**, 2229 (1914).

[3] Wohl, Ber. **31**, 1799 (1898); Evans and Hass, J. Am. Chem. Soc. **48**, 2706 (1926); Witzemann, J. Am. Chem. Soc. **36**, 1912 (1914); Spoehr and Young, Carnegie Inst. Washington Yearbook, **25**, 177 (1925–1926); Expt. Sta. Record, **57**, 817 (1927) [C. A. **22**, 2368 (1928)].

XVIII

HEPTALDOXIME

$$2CH_3(CH_2)_5CHO + 2NH_2OH \cdot HCl + Na_2CO_3 \rightarrow$$
$$2CH_3(CH_2)_5CH{=}NOH + 2NaCl + CO_2 + 3H_2O$$

Submitted by E. W. Bousquet.
Checked by W. H. Carothers and W. L. McEwen.

1. Procedure

In a 5-l. two-neck flask, fitted with a mechanical stirrer, a reflux condenser, a thermometer and a separatory funnel, are placed an aqueous solution of 348 g. (5 moles) of hydroxylamine hydrochloride (Org. Syn. **3**, 61) in 600 cc. of cold water and 460 g. (4 moles) of heptaldehyde (Note 1). Stirring (Note 2) is started, and to the above mixture a solution of 265 g. (2.5 moles) of anhydrous sodium carbonate (c. p. grade) in 500 cc. of water is added at such a rate that the temperature of the reaction mixture does not rise above 45°. Stirring is continued at room temperature for an hour after the addition of the sodium carbonate solution is complete.

The oily layer on top of the reaction mixture is separated and washed with two 100-cc. portions of water (Note 3). The washed product is transferred to a 1.5-l. modified Claisen flask (Org. Syn. **1**, 40) and distilled under reduced pressure from an oil bath. The first fraction contains a very small amount of water along with a mixture of heptanonitrile and heptaldoxime. The product is collected at 103–107°/6 mm. (temperature of the oil bath (140–147°) (Note 4). The yield is 420–480 g. (81–93 per cent of the theoretical amount). The product solidifies slowly on cooling and melts at 44–46°. It can be used directly

for reduction to *n*-heptylamine (p. 58) without further purification.

The product is purified by recrystallization from 60 per cent ethyl alcohol, using approximately 70 cc. of the solvent to 25 g. of the distilled product. One such recrystallization (Note 5) gives white leaflets melting at 53–55° (uncorr.) (Notes 6 and 7). The yield of recrystallized material from a single run is 315–320 g.

2. Notes

1. The heptaldehyde used boiled at 54–59°/16 mm.

2. Since the heptaldehyde and the aqueous solution of hydroxylamine hydrochloride form a heterogeneous mixture, it is necessary to provide rapid, efficient stirring in order to obtain good results.

Ethyl alcohol can be used to provide a homogeneous solution, but the yield seems to be diminished slightly due to the presence of more high boiling material.

3. The product is so insoluble in water that an ether extraction is hardly necessary to obtain all of the product from the water solution if sufficient time is allowed for the separation of the two layers.

4. The temperature of the oil bath during distillation is important. The first fraction is cut as soon as a constant boiling point is reached, and this constancy of boiling point is obtained sooner if the temperature of the oil bath is regulated to a constant temperature before distillation is started. No more than 50 cc. (of which approximately 10 cc. is water) should come over in the first fraction. If the temperature of the bath is regulated carefully, practically all of the product will distil at a constant temperature.

5. The product is dissolved by gentle heating and the solution is then cooled to 0° or below for several hours. The material remaining in the mother liquor (about 30 per cent of the total) may be recovered as impure, oily oxime by evaporation of the alcohol.

6. The melting point given was determined by the capillary

tube method and depended on the rate of heating. The melting point is given in the literature at temperatures varying from 50° to 58°.

7. Cyclohexanoneoxime can be prepared in the same percentage yields by a procedure which differs from the above only in that the reaction mixture becomes solid before the addition of the sodium carbonate is complete. After all of the sodium carbonate has been added, steam is passed in until the oxime is melted, and the mixture is shaken vigorously for fifteen minutes at five-minute intervals. Cyclohexanoneoxime boils at 100–105°/10–12 mm. and melts at 87–88°.

3. Methods of Preparation

Heptaldoxime has been prepared only by the action of the aldehyde on an aqueous solution of hydroxylamine hydrochloride in the presence of alkali,[1] and the method described above is a modification of that given by Westenberger.[2]

[1] Westenberger, Ber. **16**, 2992 (1883); Goldschmidt and Zanoli, Ber. **25**, 2593 (1892); Bourgeois and Dambmann, Ber. **26**, 2860 (1893).

[2] Westenberger, Ber. **16**, 2992 (1883).

XIX

n-HEPTYLAMINE

$$CH_3(CH_2)_5CH{=}NOH + 4[H](Na + C_2H_5OH) \rightarrow CH_3(CH_2)_6NH_2 + H_2O$$

Submitted by W. H. Lycan, S. V. Puntambeker, and C. S. Marvel.
Checked by W. H. Carothers and W. L. McEwen.

1. Procedure

A solution of 258 g. (2 moles) of heptaldoxime (p. 54) in 4 l. of absolute alcohol (Note 1) is heated to boiling in a 12-l. round-bottom flask on a steam bath. The flask is equipped with a 150-cm. reflux condenser in which the inner tube is very wide (2.5 cm.). As soon as the alcohol begins to boil, the steam is shut off and the temperature is maintained by introducing strips of sodium through the top of the condenser. The total amount of sodium added is 500 g., and it should be added as rapidly as is possible without loss of alcohol (Note 2). The last 150 g. of sodium melts in the hot mixture and may be added very rapidly without loss of alcohol or amine.

As soon as the sodium has dissolved, the contents of the flask are cooled and diluted with 5 l. of water. The flask is equipped at once with a condenser set for distillation and the distillate is carried below the surface of a solution of 300 cc. of concentrated hydrochloric acid in 300 cc. of water in a second 12-l. flask. The distillation is continued as long as any basic material passes over. When frothing interferes toward the end of the distillation an additional 3 l. of water is added to the distillation flask. The total distillate is 8–9 l.

The alcohol, water and unreacted oxime are removed by distillation under reduced pressure (about 20–30 mm.) from the

steam cone and the amine hydrochloride crystallizes in the flask. The flask is then cooled and equipped with a reflux condenser through which 1 l. of 40 per cent potassium hydroxide solution is introduced. The hydrochloride is washed down from the sides of the flask, and the resulting mixture is cooled and transferred to a separatory funnel. The lower alkaline layer is removed and solid potassium hydroxide is added to the amine in the funnel. Twenty-four to thirty hours are required for complete drying. The aqueous layer is removed and fresh sticks of potassium hydroxide are added from time to time until no further separation of an aqueous alkaline solution occurs. The amine is then decanted through the top of the funnel into a 250-cc. modified Claisen flask (Org. Syn. 1, 40) and distilled. The *n*-heptylamine is collected at 152–157°. The yield is 140–170 g. (60–73 per cent of the theoretical amount) (Note 3).

2. Notes

1. The yields are poor if the alcohol is not completely dehydrated. A very satisfactory grade of alcohol is obtained by distilling ordinary absolute alcohol from magnesium methylate (Org. Syn. 7, 37).

2. The best yields are obtained when the reduction is carried out rapidly.

3. Using essentially the same method the following amines have been prepared in 50–60 per cent yields: *n*-butylamine, b. p. 75–80°, from butyraldoxime; *sec.*-butylamine, b. p. 59–65° from ethylmethyl ketoxime; cyclohexylamine, b. p. 133–135°, from cyclohexanoneoxime. Greater care must be observed in drying the butylamines.

3. Methods of Preparation

n-Heptylamine has been prepared by the reduction of 1-nitroheptane with iron and acetic acid;[1] by the reduction of heptaldoxime with sodium amalgam and acetic acid;[2] by the

[1] Worstall, Am. Chem. J. **21**, 223 (1899).
[2] Goldschmidt, Ber. **20**, 729 (1887).

reduction of heptaldoxime with hydrogen in the presence of a nickel catalyst;[3] by the reduction of the phenylhydrazone of heptaldehyde with sodium amalgam and acetic acid;[4] by the reduction of heptanonitrile with sodium and alcohol;[5] by the reduction of heptanoamide with sodium and amyl alcohol;[6] from methyl *n*-heptyl ketoxime by the Beckmann rearrangement followed by hydrolysis;[7] by the action of potassium hypobromite on the amide of caprylic acid;[8] by the reduction of heptanonitrile with hydrogen in the presence of a nickel catalyst;[9] and by the reduction of a solution of heptaldehyde and ammonia in alcohol with hydrogen in the presence of a nickel catalyst.[10]

The method described in the procedure is the method generally used for the reduction of oximes by means of sodium and alcohol.

[3] Mailhe, Compt. rend. **140**, 1692 (1905); Bull. soc. chim. (3) **33**, 963 (1905); Sabatier and Mailhe, Ann. chim. phys. (8) **16**, 102 (1909).

[4] Tafel, Ber. **19**, 1928 (1886).

[5] Forselles and Wahlforss, Ber. **25**, 637 (abstracts) (1892).

[6] Scheuble and Loebl, Monatsh. **25**, 1087 (1904).

[7] von Soden and Henle, Chem. Zentr. **1902**, I, 256.

[8] Hofmann, Ber. **15**, 771 (1882); Hoogewerff and van Dorp, Rec. trav. chim. **6**, 386 (1887).

[9] Mailhe and de Godon, Bull. soc. chim. (4) **23**, 19 (1918); Mailhe and Bellegarde, Bull. soc. chim. (4) **25**, 591 (1919); Mailhe, Ann. chim. phys. (9) **13**, 203 (1920).

[10] Mignonac, Compt. rend. **172**, 226 (1921).

XX

p-IODOANILINE

$$C_6H_5NH_2+I_2+NaHCO_3 \rightarrow p\text{-}IC_6H_4NH_2+NaI+H_2O+CO_2$$

Submitted by R. Q. Brewster.
Checked by W. H. Carothers and W. L. McEwen.

1. Procedure

In a 3-l. beaker are placed 110 g. (1.2 moles) of aniline, 150 g. (1.76 moles) of sodium bicarbonate and 1 l. of water, and the mixture is cooled to 12–15° by the addition of a small amount of ice. The beaker is then fitted with an efficient mechanical stirrer. The blade of a large porcelain spatula should be inserted into the liquid to overcome the rotary motion and thus obtain better mixing. The stirrer is started and 254 g. (1 mole) of powdered iodine is added in 15–20 g. portions at intervals of two to three minutes so that all the iodine is introduced during the course of one-half hour. Stirring is continued for twenty to thirty minutes. By this time the reaction is complete, and the color of the free iodine in the solution has practically disappeared. The crude *p*-iodoaniline, which separates as a dark crystalline mass, is collected on a Büchner funnel, pressed as free from water as possible, and dried in the air. The filtrate may be saved for the recovery of iodine (Note 1).

For the purification of the *p*-iodoaniline, the crude product is placed in a 2-l. flask and 1 l. of gasoline (Note 2) is added. The flask is fitted with an air-cooled reflux condenser and heated in a water bath at a temperature of 75–80° (Note 3). The flask should be shaken frequently and about fifteen minutes

should be allowed for saturation of the solution. The hot gasoline solution is slowly decanted into a beaker set in an ice-salt mixture and stirred constantly. The *p*-iodoaniline crystallizes immediately in practically colorless needles which are filtered and dried in the air (Notes 4 and 5). The filtrate is returned to the flask for use in a second extraction (Note 6). The yield is 165–185 g. (75–84 per cent of the theoretical amount) of a product which melts at 62–63°.

2. Notes

1. The sodium iodide which remains in the aqueous solution may be converted into iodine as follows: To the aqueous filtrate from the *p*-iodoaniline are added 100 cc. of concentrated sulfuric acid and 200 g. of sodium dichromate in 200 cc. of water. The iodine is allowed to settle, washed three times with water by decantation, collected on a filter, and allowed to dry on a watch glass. The yield of crude iodine is 167–179 g.

2. The gasoline used was a fractionated product (b. p. 70–150°). Ordinary gasoline may be used, but it has the disadvantage that the higher boiling hydrocarbons are removed very slowly from the *p*-iodoaniline.

3. If a higher temperature is used a tarry material is sometimes formed and a diminished yield results.

4. If rapid cooling is not obtained, the product often separates as an oil.

5. For drying purposes, a current of warm air from a commercial hair dryer is advantageous.

6. Two extractions are usually sufficient, but if much undissolved organic material still remains, a third extraction should be made. The first fraction is practically colorless, but the second and third portions are light brown unless a little charcoal is used for decolorization of the solution.

3. Methods of Preparation

p-Iodoaniline has been prepared by the reduction of *p*-nitroiodobenzene;[1] by the hydrolysis of *p*-iodoacetanilide formed by the action of iodine monochloride on acetanilide;[2] and by the direct iodination of aniline.[3] The method described here is an adaptation of the procedure used by Wheeler,[4] and by Hann and Berliner [5] for the iodination of the toluidines.

[1] Griess, Zeit. f. Chem. **1866**, 218; Kekulé, *ibid.* 687; Körner and Wender, Gazz. chim. ital. **17**, 489 (1887); Baeyer, Ber. **38**, 2762 (1905); Montagne, Ber. **51**, 1490 (1918).

[2] Michael and Norton, Ber. **11**, 108 (1878); Chattaway and Constable, J. Chem. Soc. **105**, 125 (1914).

[3] Hofmann, Ann. **67**, 65 (1848); Bradfield, Orton and Roberts, J. Chem. Soc. **1928**, 783.

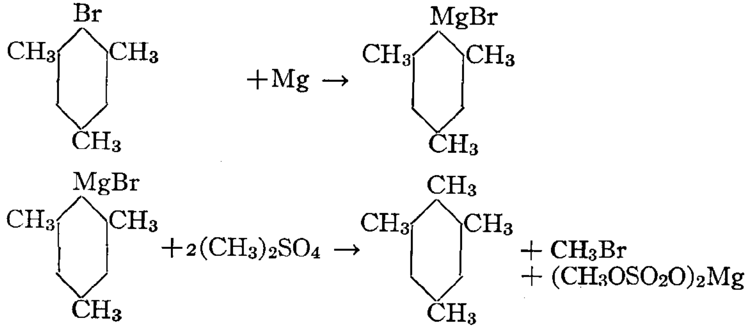
[4] Wheeler and Liddle, Am. Chem. J. **42**, 501 (1909); Wheeler, Am. Chem. J. **44**, 128, 500 (1910).

[5] Hann and Berliner, J. Am. Chem. Soc. **47**, 1710 (1925).

XXI

ISODURENE

(1,2,3,5-*Tetramethylbenzene*)



Submitted by LEE IRVIN SMITH.
Checked by ROGER ADAMS and W. W. MOYER.

1. Procedure

A 3-l. three-neck flask, fitted with a reflux condenser protected from the air by a calcium chloride tube, a separatory funnel and a mechanical stirrer, is mounted on a steam bath. In this flask are placed 48 g. (2 moles) of magnesium turnings, 150 cc. of anhydrous ether and 100 g. of bromomesitylene (p. 24). The reaction starts slowly and sometimes it is necessary to add some iodine or use Gilman's catalyst (Note 1). After the reaction starts, it proceeds smoothly and the remaining 298 g. of bromomesitylene (a total of 2 moles) in about 700 cc. of dry ether is added at such a rate that the ether boils briskly. After the last of this ether solution has been added, the mixture is heated on the steam cone until practically all of the magnesium has dissolved (Note 2).

The solution of the Grignard reagent is cooled to about 10°. To the vigorously stirred solution is added a solution of 600 g. (4.8 moles) of dimethyl sulfate (Note 3) in about 500 cc. of dry ether. The reaction is very vigorous and bumping may occur due to the separation of insoluble magnesium compounds. The addition of the dimethyl sulfate requires from two to three hours. The reaction mixture is allowed to stand (Note 4) for about twenty-four hours and is then decomposed by adding dilute hydrochloric acid through the separatory funnel. Stirring is started as soon as the mass is fluid enough. When the mixture is decomposed completely, the ether layer is separated and washed three times with water. After the magnesium salts have been removed, the ether layer is evaporated and the residue is added slowly to a solution of 30 g. of sodium in 500 cc. of absolute alcohol (Note 5). The mixture is boiled for about one-half hour. Then the solution is cooled, 150–200 cc. of ether is added and the alkali and alcohol are removed by washing thoroughly with water (Note 6). Finally the ether solution is dried over calcium chloride, the ether is distilled and the residue is warmed on a water bath from three to four hours with 25–30 g. of metallic sodium (Note 7). The mixture is filtered and the filtrate is fractionated carefully under reduced pressure in a modified Claisen flask (Org. Syn. 1, 40). The fractions collected are: up to 85°/18 mm.; 85–87°/18 mm.; and residue. The low-boiling fraction weighs about 50 g. and is mainly mesitylene. The second fraction is isodurene and has a melting point of −24.2°. The yield is 140–160 g. (53–61 per cent of the theoretical amount).

2. Notes

1. Gilman's catalyst [1] is prepared readily by heating an alloy of magnesium containing 12.75 per cent of copper with about 20 per cent by weight of iodine in an evacuated flask. Only about 0.25 g. of this catalyst is required to bring about a reaction with a halogen compound. When this catalyst is used, the

[1] Gilman, Peterson, and Schulze, Rec. trav. chim. 47, 19 (1928).

ordinary magnesium turnings are added as soon as the reaction has started. The reaction can also be started by adding a small amount of an ether solution of any Grignard reagent, such as ethyl-magnesium bromide.

2. If Gilman's catalyst is used to start the reaction there will always be an excess of magnesium at the end of the reaction.

3. The dimethyl sulfate was distilled carefully under reduced pressure, and a 1° fraction was used in this preparation. Dimethyl sulfate is extremely toxic and great care must be taken to avoid breathing the vapors and spilling the liquid on the hands or clothes.

4. The reaction mixture sometimes becomes almost solid, and then stirring is useless in the later stages.

5. Aqueous alkali is not sufficient to remove the excess dimethyl sulfate. Sometimes the reaction between the excess dimethyl sulfate and the sodium ethylate solution is vigorous, so the mixing of the two solutions should be done with some care. If a large excess of dimethyl sulfate is present, more sodium ethylate may be needed in order to keep the solution alkaline.

6. If emulsions form, they may be broken by acidifying the product.

7. The treatment with sodium insures a halogen-free product.

3. Methods of Preparation

Isodurene has been prepared from bromomesitylene, methyl iodide and sodium;[2] from mesitylene, methyl chloride and aluminum chloride;[3] from mesitylene, methyl iodide, aluminum chloride and carbon disulfide;[4] from 1,3,4,5-tetramethyl benzonitrile with hydrogen chloride at 250°;[5] by the action of zinc chloride or iodine on camphor;[6] and in small amounts by the

[2] Jannasch, Ber. **8**, 356 (1875); Bielefeldt, Ann. **198**, 380 (1879); Jannasch and Weiler, Ber. **27**, 3442 (1894).

[3] Jacobsen, Ber. **14**, 2629 (1881).

[4] Claus and Foecking, Ber. **20**, 3097 (1887).

[5] Hofmann, Ber. **17**, 1915 (1884).

[6] Armstrong and Miller, Ber. **16**, 2259 (1883).

action of concentrated sulfuric acid on acetone.[7] The above method of preparation has been described recently.[8]

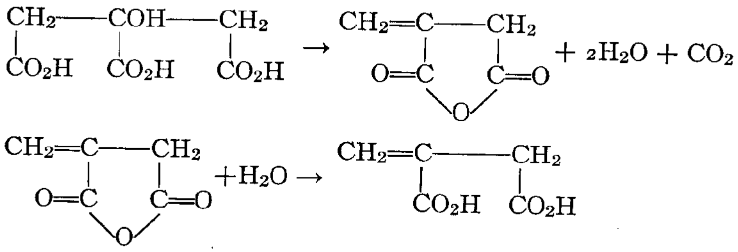
No method in which aluminum chloride is used will give a pure product, for aluminum chloride shifts the methyl groups so that the three tetramethylbenzenes always result. These cannot be separated efficiently by any known method.

[7] Orndorff and Young, Am. Chem. J. **15**, 267 (1893).

[8] Smith and MacDougall, J. Am. Chem. Soc. **51**, 3003 (1929).

XXII

ITACONIC ANHYDRIDE AND ITACONIC ACID



Submitted by R. L. Shriner, S. G. Ford, and L. J. Roll.
Checked by C. R. Noller.

1. Procedure

A. *Itaconic Anhydride:* A 500-cc. Pyrex Kjeldahl flask is fitted with an outlet tube 12 mm. in diameter bent for downward distillation. It is attached to a 100-cm. water-cooled condenser having an indented Pyrex inner tube (Note 1). Two 250-cc. long-neck distilling flasks are used in series as receivers, the vapors being led to the center of each flask by means of an adapter and glass tubing. Both receivers are cooled in a mixture of ice and water.

Two hundred grams of citric acid (0.95 mole) (Note 2) is placed in the reaction flask (Note 3) and heated with a free flame until melted. Then the flask is heated very rapidly with a large Meker burner, and the distillation is completed as rapidly as possible (ten to twelve minutes). Care must be taken to avoid superheating (Note 4). The distillate consists of water and itaconic anhydride, most of which distils at 175–190°. The distillate is immediately (Note 5) poured into a separatory

funnel and the lower layer of itaconic anhydride is separated (Note 6). The yield of the anhydride is 40–50 g. (37–47 per cent of the theoretical amount). It is of sufficient purity for use in the preparation of citraconic anhydride (p. 28) (Note 7).

B. *Itaconic Acid:* Forty grams of itaconic anhydride is refluxed with 100 cc. of water for one hour. The flask is then set aside to cool, and finally placed in an ice bath. The acid crystallizes and is filtered and dried. The yield is 11–18 g. (24–39 per cent of the theoretical amount) of a product which melts at 162–165°. On concentrating the mother liquor to one-third of the original volume, an additional amount of lower-melting product may be obtained (Note 8).

2. Notes

1. A Pyrex inner tube is recommended, since the rapid stream of hot vapor often cracks a soft glass tube. A suitable tube may be prepared from a piece of ordinary Pyrex tubing of the proper size by softening it in spots in the blast lamp and applying suction.

2. The citric acid used was a U.S.P. grade containing one molecule of water of crystallization. The use of larger amounts of citric acid usually results in a lower yield.

3. A clean flask should be used for each run since the presence of residue from a previous run causes excessive foaming during the first part of the decomposition. The flask is cleaned most easily by adding a 25 per cent solution of sodium hydroxide while the residue at the bottom is still molten. Further heating brings about complete solution.

4. Superheating tends to increase the rearrangement to citraconic anhydride. The flask should be heated on all sides over a considerable area. The distillation should be stopped as soon as the vapors in the reaction flask become yellow.

5. Prolonged standing in contact with the water layer causes partial hydrolysis.

6. The water layer may be concentrated to give a mixture of itaconic and citraconic acids.

7. The purity of the itaconic anhydride seems to vary greatly with the conditions of the experiment. The crude anhydride always deposits crystals of itaconic acid on standing, probably due to water dissolved or suspended in the anhydride. Some idea of the purity can be obtained by the quantity of itaconic acid that is obtained from it. If the distillation proceeds at exactly the right rate, the anhydride is pure and melts at 67–68°.

8. In some cases no itaconic acid crystallizes. This apparently happens when the distillation of the citric acid has not been carried out rapidly enough and the itaconic anhydride contains a large amount of citraconic anhydride.

3. Methods of Preparation

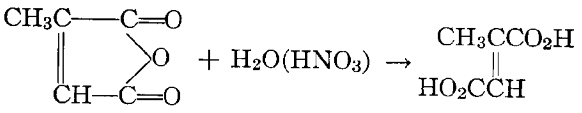
Itaconic anhydride has been made by heating itaconic acid and by distillation of citric acid.[1]

Itaconic acid has been prepared by the distillation of citric acid,[2] of aconitic acid,[3] and of itamalic acid;[4] by heating citric acid with dilute sulfuric acid in a closed tube;[5] by treating aconitic acid with water at 180°;[6] by heating citraconic acid with sodium hydroxide;[7] by heating citraconic anhydride with water at 150°;[8] and by heating a concentrated solution of citraconic acid at 120–130° in a sealed tube.[9]

[1] Anschütz, Ber. **13**, 1541 (1880).
[2] Baup, Ann. **19**, 29 (1836).
[3] Crasso, Ann. **34**, 63 (1840).
[4] Swarts, Zeit. f. Chem. **3**, 649 (1867).
[5] Markownikow and von Purgold, Zeit. f. Chem. **3**, 264 (1867).
[6] Pebal, Ann. **98**, 94 (1856).
[7] Delisle, Ann. **269**, 86 (1893).
[8] Fittig, Ann. **188**, 72 (1877).
[9] Wilm, Ann. **141**, 29 (1867).

XXIII

MESACONIC ACID



Submitted by R. L. Shriner, S. G. Ford and L. J. Roll.
Checked by C. R. Noller.

1. Procedure

A mixture of 100 g. (0.88 mole) of citraconic anhydride (p. 28) (Note 1), 100 cc. of water, and 150 cc. of dilute nitric acid (1 part of concentrated nitric acid to 4 parts of water by volume) is evaporated in a 500-cc. Erlenmeyer flask until the appearance of red fumes (Note 2). The solution is cooled and the mesaconic acid is collected on a filter. The mother liquor is evaporated to 150 cc., cooled, and the crystalline solid which separates is collected on a filter. Further concentration of the mother liquor to 50 cc. yields more product (Note 3). The entire product is recrystallized from 100 cc. of water. The yield of product melting at 203–205° is 50–60 g. (43–52 per cent of the theoretical amount).

2. Notes

1. Either the acid or the anhydride may be used.

2. It is necessary to carry the evaporation to the point where red fumes appear in order for the rearrangement to take place. The volume is usually about 250 cc.

3. The concentration of the mother liquor must be carried out in steps in order to obtain an efficient separation of mesaconic acid.

3. Methods of Preparation

Mesaconic acid has been prepared by heating citraconic acid with dilute nitric acid,[1] with hydriodic acid,[2] or with concentrated sodium hydroxide solution;[3] by heating a concentrated water solution of itaconic or citraconic acid at 180–200°;[4] by treating citradibromopyrotartaric acid and mesodibromopyrotartaric acid with potassium iodide and copper at 150°;[5] and by heating citraconic anhydride with nitric acid.[6]

[1] Gottlieb, Ann. **77**, 268 (1851).
[2] Kekulé, Ann. Spl. **2**, 94 (1863).
[3] Delisle, Ann. **269**, 82 (1893).
[4] Swarts, Jahresber. **1873**, 579.
[5] Swarts, Zeit. f. Chem. **1868**, 259.
[6] Fittig, Ann. **188**, 73 (1877).

XXIV

3-METHYL PENTANOIC ACID

$$CH_3CH_2CH(CH_3)CH(CO_2C_2H_5)_2 + 2KOH \rightarrow CH_3CH_2CH(CH_3)CH(CO_2K)_2 + 2C_2H_5OH$$

$$CH_3CH_2CH(CH_3)CH(CO_2K)_2 + H_2SO_4 \rightarrow CH_3CH_2CH(CH_3)CH_2CO_2H + CO_2 + K_2SO_4$$

Submitted by E. B. Vliet, C. S. Marvel, and C. M. Hsueh.
Checked by Henry Gilman and R. E. Brown.

1. Procedure

A solution of 200 g. (3.57 moles) of potassium hydroxide (Note 1) in 200 cc. of water is placed in a 2-l. round-bottom flask fitted with a reflux condenser, a mechanical stirrer and a separatory funnel. The stirrer is started and to the hot solution 200 g. (0.92 mole) of ethyl *sec.*-butylmalonate (Note 2) is added slowly. The solution refluxes gently due to the heat of saponification. After all of the *sec.*-butylmalonic ester has been added, the solution is refluxed gently for two hours. The solution is diluted with 200 cc. of water and 200 cc. of liquid is then distilled from the solution. This is done in order to remove all of the alcohol formed during the saponification (Note 3).

The solution is allowed to cool and a cold solution of 320 g. (3.3 moles) of concentrated sulphuric acid (Note 4) in 450 cc. of water is added through the separatory funnel. This should be done slowly and with stirring in order to prevent foaming. The solution becomes hot and may reflux spontaneously. After all of the sulfuric acid has been added the solution is refluxed for about three hours. A layer of organic acid appears and the reflux condenser is replaced by an automatic separator (Org.

Syn. 1, 68) (Note 5). The solution is distilled with the separator, and the aqueous portion is returned to the distilling flask. This operation is continued until practically all of the organic acid has been driven over. This requires from ten to fifteen hours. At the end, about 100 cc. of water is collected in the separator and extracted with ether in order to remove the dissolved acid (Note 6). The ether is distilled and the crude acid is mixed with an equal volume of dry benzene (Note 7) and distilled through a fractionating column (Org. Syn. 1, 40). Benzene and water distil first and then the 3-methyl pentanoic acid distils at 193–196°/743 mm. The yield is 66–69 g. (62–65 per cent of the theoretical amount) (Note 8).

2. Notes

1. Sodium hydroxide is unsatisfactory for this saponification because an organic sodium salt separates, yielding a semi-solid mass.

2. The ethyl *sec.*-butylmalonate was prepared from *sec.*-butyl bromide and malonic ester according to the general method described in Org. Syn. 4, 11. The yield of ester boiling at 124–132°/28 mm. was 80–81 per cent of the theoretical amount. The yields of 3-methyl pentanoic acid given in this procedure were obtained with this grade of ester.

3. It is necessary that all of the alcohol be eliminated after the saponification. If some is allowed to remain, ethyl 3-methyl pentanoate is formed and a considerable amount of low-boiling material is present in the final product.

4. If hydrochloric acid is used, it distils and complicates the purification of the product.

5. Various other methods were tried for isolating the acid but none was as effective as the one described. Solvent extractions did not remove it completely; the yield was about 10 per cent less and the product was contaminated with tarry impurities.

6. The amount of acid recovered by the ether extraction is only 1–2 g.

7. The acid may be dried by other means, but this method was found most convenient.

8. Other acids may be prepared by this general procedure; thus *n*-caproic acid may be obtained from ethyl *n*-butylmalonate in 75 per cent yield.

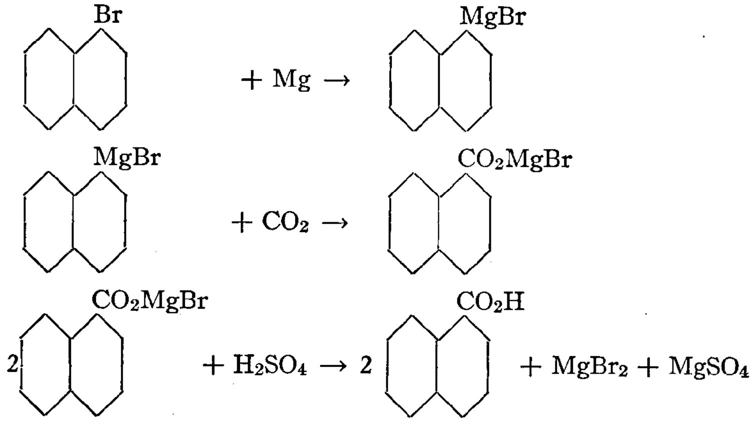
3. Methods of Preparation

3-Methyl pentanoic acid has always been prepared by heating *sec.*-butyl malonic acid.[1]

[1] Van Romburgh, Rec. trav. chim. **6**, 153 (1887); Kulisch, Monatsh. **14**, 559 (1893); Bentley, J. Chem. Soc. **67**, 267 (1895).

XXV

α-NAPHTHOIC ACID



Submitted by HENRY GILMAN, NINA B. ST. JOHN, and F. SCHULZE.
Checked by C. R. NOLLER.

1. Procedure

IN a 2-l. three-neck flask, fitted with a mechanical stirrer, a reflux condenser and a separatory funnel, is placed 24.3 g. (1 mole) of magnesium turnings (Note 1). The magnesium is covered with 100 cc. of anhydrous ether, and 10 cc. (15.0 g.; 0.07 mole) of α-bromonaphthalene (Note 2) (with a crystal or two of iodine) (Note 3) is added to start the reaction. A warm water bath (45° or higher) is placed under the flask until the reaction starts. The stirrer is started and a solution of 192 g. (0.93 mole) of α-bromonaphthalene in 500 cc. of anhydrous ether is added to the magnesium at such a rate that the reaction is vigorous but not violent. The addition requires from one and

one-half to three hours. The water bath is again placed under the flask, and stirring and refluxing are continued for one-half hour after the addition of the halide is complete. The Grignard reagent which collects as a heavy oil in the bottom of the flask is dissolved by the addition of 533 cc. of dry benzene (Note 4).

The reaction mixture is then cooled by an ice-salt mixture. The separatory funnel is replaced by a two-hole rubber stopper containing a thermometer (bulb immersed in the reaction mixture) and a glass tube drawn out to make a fine capillary (Note 5). When the temperature of the reaction mixture has reached −7°, the condenser is replaced by an entry tube, 10 mm. in diameter and adjusted so the end is about 50 mm. above the surface of the reaction mixture (Note 6). The reaction mixture is stirred, and dry carbon dioxide is added through this tube (Note 7). The rate of flow of the carbon dioxide is regulated so that the temperature of the reaction mixture does not rise above −2°. The time required for the completion of the reaction varies from one and one-fourth to one and one-half hours. When the reaction is complete, the temperature falls below −7° and does not rise on increasing the rate of flow of carbon dioxide.

The flask is placed in an ice bath and 25 per cent sulfuric acid is added slowly, with stirring, until no further reaction takes place and all of the excess magnesium has dissolved (Note 8). The oily layer is separated, and the water layer is extracted with two 100-cc. portions of ether. The combined ether-benzene extracts (Note 9) are shaken with three 100-cc. portions of 25 per cent sodium hydroxide. Each alkaline layer is extracted successively with a 100-cc. portion of ether, and the combined alkaline extracts are then heated to 100° to drive off volatile impurities.

The solution is cooled and acidified strongly with 50 per cent sulfuric acid. The crude α-naphthoic acid is collected on a Büchner funnel, washed until free from sulfate, and dried. The yield of crude material melting at 142–155° is 130–135 g. This is dissolved in 400 cc. of hot toluene, a small amount of filter-cel is added, and the solution is filtered through a hot Büchner fun-

nel. The filtrate is cooled in an ice bath, filtered with suction, and the filter cake washed with cold toluene until the filtrate is practically colorless. A light-colored product melting at 159–161° is obtained. The yield is 118–121 g. (68–70 per cent of the theoretical amount) (Note 10).

2. Notes

1. The finer commercial grade of turnings was used. After the reaction had once started, it proceeded smoothly with any grade of commercial turnings.

2. The α-bromonaphthalene (Org. Syn. **1**, 35; **10**, 14) was purified by distillation under reduced pressure. The fraction boiling at 144–147°/16 mm. was collected.

3. The checker was more successful in starting the reaction within a reasonable length of time when as much as 0.5 g. of iodine was added.

4. It is necessary to dissolve the Grignard reagent in benzene to prevent it from solidifying when the solution is cooled. The benzene should be added to the solution before it cools, as the hardened mass is difficult to redissolve.

5. This is to allow the carbon dioxide which does not react to escape slowly in order that the pressure in the flask does not become too great.

6. The inlet tube is placed at this distance above the surface of the reaction mixture in order to prevent clogging.

7. The carbon dioxide from an ordinary commercial cylinder was dried by passing it through two wash bottles containing sulfuric acid.

8. Cooling the solution externally with ice permits the rapid hydrolysis without danger of loss of material through refluxing (cf. Gilman and Parker, Org. Syn. **5**, 75).

9. If the ether-benzene solution is not entirely clear, it should be filtered before extraction with sodium hydroxide.

10. A second recrystallization from toluene gives an almost white product melting at 160.5–162°.

3. Methods of Preparation

α-Naphthoic acid has been prepared by the hydrolysis of α-naphthyl cyanide [1] and (in poor yield) by the fusion of sodium α-naphthalenesulfonate and sodium formate.[2] It has also been prepared by passing carbamyl chloride into naphthalene and aluminum chloride and hydrolyzing the α-napthamide thus formed.[3]

The above procedure [4] was developed from the methods of Acree,[5] of Blicke,[6] and of Whitmore and Fox.[7]

[1] Merz and Mülhaüser, Ber. **3**, 712 (1870).
[2] Meyer, Ber. **3**, 364 (1870).
[3] Gattermann and Schmidt, Ber. **20**, 860 (1887).
[4] Gilman, St. John and St. John, Rec. trav. chim. **48**, 594 (1929).
[5] Acree, Ber. **37**, 625 (1904).
[6] Blicke, J. Am. Chem. Soc. **49**, 2846 (1927).
[7] F. C. Whitmore and A. L. Fox, *private communication.*

XXVI

n-PENTANE

$$CH_3(CH_2)_2CHBrCH_3 + Mg \rightarrow CH_3(CH_2)_2CH(MgBr)CH_3$$

$$2CH_3(CH_2)_2CH(MgBr)CH_3 + H_2SO_4 \rightarrow$$

$$2CH_3(CH_2)_3CH_3 + MgBr_2 + MgSO_4$$

Submitted by C. R. Noller.
Checked by Roger Adams and L. J. Roll.

1. Procedure

In a 5-l. flask, placed on a steam bath and fitted with a mechanical stirrer, a separatory funnel, a thermometer well (Note 1) and a calcium chloride tube, is placed 182 g. (7.5 moles) of magnesium turnings. To this is added a crystal of iodine and 100 cc. of a solution of 1133 g. (7.5 moles) of 2-bromopentane (Note 2) in 750 g. of *n*-butyl ether (Note 3). The stirrer is started and the flask is heated with steam until the reaction starts. This may take from fifteen minutes to one hour, but the flask must be watched quite closely because the reaction, when once started, is very vigorous and evolves a large amount of heat. As soon as the reaction has started, 750 g. of *n*-butyl ether is added and then the balance of the solution of 2-bromopentane in *n*-butyl ether is added at such a rate that the temperature is kept at 50–60°. External cooling is used in order to allow more rapid addition of the 2-bromopentane. After addition is complete (about three hours), the mixture is heated on a steam bath for one hour.

In the meantime, a 12-l. flask containing a solution of 450 cc. of concentrated sulfuric acid in 3 l. of water is placed on a steam bath and fitted with a stirrer, a separatory funnel and

an efficient ice-cooled condenser set for distillation. The stirrer is started and the solution of the Grignard reagent, prepared above, is added. The acid solution is allowed to become warm but is kept below the boiling-point by external cooling. After all the Grignard reagent has been added, the mixture is heated on the steam bath until no more pentane distils. The reaction flask is allowed to cool, and the *n*-butyl ether layer is separated, transferred to a 5-l. flask connected with the condenser and heated with a free flame until the boiling-point of the *n*-butyl ether is reached (Note 4). The combined distillate is separated from a small amount of water, washed twice with 125-cc. portions of cold, concentrated sulfuric acid and allowed to stand overnight with anhydrous potassium carbonate. After removing the potassium carbonate, the *n*-pentane is fractionated twice through an efficient 100-cm. fractionating column. The yield is 270–290 g. (50–53 per cent of the theoretical amount) of a product which boils at 35.5–36.5°.

2. Notes

1. A closed glass tube containing mercury was used as a thermometer well. It was inserted with the end in the reaction mixture. The thermometer was placed in the well with the bulb in the mercury.

2. The 2-bromopentane used in this preparation was prepared by the action of hydrobromic acid on secondary amyl alcohol (methyl *n*-propyl carbinol) obtained from Stanco Distributors, Inc. Other commercial straight chain amyl alcohols when converted to the bromides gave a pentane boiling at 33–35°, showing that a considerable quantity of iso-pentane was present.

3. The use of *n*-butyl ether allows the ready separation of the pentane by distillation. The butyl ether used in this preparation boiled at 142–144°.

4. About 70 per cent of the *n*-butyl ether is recovered readily and may be purified by distillation.

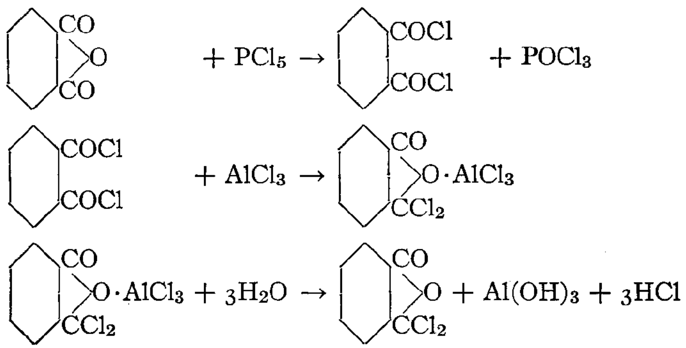
3. Methods of Preparation

n-Pentane has been obtained from petroleum,[1] from Boghead and Cannel coals,[2] and from rosin oils.[3] It has been prepared by heating hexane with aluminum chloride;[4] by heating acetylacetone with concentrated hydriodic acid at 180°;[5] by heating pyridine with concentrated hydriodic acid above 300°;[6] and by heating diethyl ketone with hydrazine hydrate at about 200°.[7] It is formed to a slight extent when di-*n*-amylamine or tri-*n*-amylamine vapor is passed over nickel at 360–370°.[8] It has also been prepared by the catalytic reduction of pyridine using colloidal platinum and hydrogen at 50°;[9] by the reduction of *n*-amylene using nickel formate and hydrogen at 120°;[10] by the reduction of 2-bromopentane using zinc dust and hydrochloric acid;[11] and by the action of water on *n*-amylmagnesium fluoride.[12] The use of *n*-butyl ether in this preparation was suggested by the paper of Marvel, Blomquist and Vaughn.[13]

[1] Pelouze and Cahours, Jahresber. **1863**, 524; Lachowicz, Ann. **220**, 190 (1883); Young, J. Chem. Soc. **71**, 440 (1897).
[2] Williams, J. Chem. Soc. **15**, 133 (1862); Schorlemmer, Ann. **125**, 105 (1863).
[3] Renard, Ann. chim. phys. (6) **1**, 225 (1884).
[4] Friedel and Gorgeu, Compt. rend. **127**, 593 (1898).
[5] Combes, Ann. chim. phys. (6) **12**, 233 (1887).
[6] Hofmann, Ber. **16**, 590 (1883).
[7] Staudinger and Kupfer, Ber. **44**, 2206 (1911).
[8] Mailhe, Compt. rend. **166**, 997 (1918); Ann. chim. phys. (9) **13**, 193 (1920).
[9] Skita and Brunner, Ber. **49**, 1598 (1916).
[10] Ger. pat. 329,471 [Frdl. **13**, 178 (1923)].
[11] Clarke and Talbot, unpublished results.
[12] Swarts, Chem. Zentr. **1921**, III, 1457.
[13] Marvel, Blomquist and Vaughn, J. Am. Chem. Soc. **50**, 2810 (1928).

XXVII

SYMMETRICAL AND UNSYMMETRICAL *o*-PHTHALYL CHLORIDES



Submitted by ERWIN OTT.
Checked by HENRY GILMAN and F. J. PROCHASKA.

1. Procedure

A. *Symmetrical o-Phthalyl Chloride:* A mixture of 148 g. (1 mole) of phthalic anhydride (Note 1) and 220 g. (1.06 moles) of phosphorus pentachloride (Note 2) is placed in a 500-cc. Claisen flask. The flask is equipped with a reflux condenser, the upper end of which is provided with a calcium chloride tube, and the side-arm of the flask is closed with a cork. The flask is inclined slightly so that any phosphorus oxychloride which collects in the stoppered side-arm will run back into the flask. After heating in an oil bath at 150° for twelve hours, the air condenser and the stopper in the end of the side-arm are removed, and the flask is connected to a water-cooled condenser. The temperature is then raised gradually to 250°, during which

time most of the phosphorus oxychloride distils into a receiver. The liquid residue is distilled under reduced pressure; at first a small quantity of phosphorus oxychloride distils, and then the *sym.-o*-phthalyl chloride distils at 131–133°/9–10 mm. The product thus obtained contains a small amount of phthalic anhydride; it solidifies on cooling in an ice-salt mixture and melts at 11–12° (Note 3). The yield is 187 g. (92 per cent of the theoretical amount).

B. *Unsymmetrical o-Phthalyl Chloride:* A mixture of 105 g. of the symmetrical *o*-phthalyl chloride and 75 g. of finely ground aluminum chloride (Note 4) is heated on a steam bath for eight to ten hours, with exclusion of moisture. The mixture should be stirred frequently until all the powder has dissolved. Upon cooling there is formed a hard mass which is broken into small pieces while still warm. When thoroughly cool, it is triturated with pieces of ice in a mortar, working with small amounts at a time. The white sediment which results is collected on a Büchner funnel and dissolved immediately in about 300 cc. of warm benzene (40–50°). The benzene solution is separated from the small aqueous layer, dried over calcium chloride for eight hours, and filtered. The benzene is distilled under reduced pressure by heating in a water bath at 30–40°. The crystalline residue is extracted in a Soxhlet apparatus with petroleum ether (b. p. 20–40°) until the residue in the thimble consists of practically pure phthalic anhydride (Note 5). The petroleum ether is distilled from the extract and the crude unsymmetrical phthalyl chloride is purified by fractional crystallization from petroleum ether (b. p. 20–50°). The purified chloride melts at 87–89°. The melting point is not sharp because the unsymmetrical compound begins to reconvert into the isomeric form. The yield of pure unsymmetrical phthalyl chloride is about 76 g. (72 per cent of the theoretical amount) and is dependent on the quality of the aluminum chloride used.

2. Notes

1. A good grade of sublimed phthalic anhydride should be used (m. p. 128–129°). If this cannot be obtained the ordinary phthalic anhydride can be purified by sublimation.

2. The phosphorus pentachloride should be freed of any phosphorus trichloride or oxychloride present. This may be done by placing the pentachloride in a flask connected to an ice-cooled receiver and heating on a water bath. The pressure in the apparatus is reduced as much as possible by means of a water pump. A calcium chloride tube should be inserted between the pump and the receiver.

3. Pure symmetrical *o*-phthalyl chloride cannot be obtained, even by recrystallization from carbon tetrachloride. A product melting at 16° may be obtained by distilling the unsymmetrical phthalyl chloride at atmospheric pressure.

4. A good quality of aluminum chloride must be used. If this is not available, it may be prepared by heating dried aluminum granules in a current of pure, dry hydrogen chloride. The gas is dried thoroughly by passing it through a tube containing phosphorus pentoxide spread on glass wool. Access of moisture to the aluminum chloride while weighing and pulverizing should be avoided as far as possible.

5. The extraction requires from eight to ten hours. The residue should be practically pure phthalic anhydride (m. p. 126°).

3. Methods of Preparation

Symmetrical *o*-phthalyl chloride has been prepared by heating phthalic anhydride and phosphorus pentachloride in sealed tubes.[1] This method is not convenient for the preparation of large quantities.

Attempts have been made to prepare pure symmetrical *o*-phthalyl chloride by repeatedly heating the crude chloride,

[1] Claus and Hoch, Ber. **19**, 1187 (1886).

still containing phthalic acid, with small amounts of phosphorus pentachloride.[2]

Conversion of the symmetrical chloride into the unsymmetrical isomer can also be effected by heating with tin tetrachloride.[3] The yield, however, is not satisfactory.

[2] Brühl, Ann. **235**, 13 (1886).
[3] Csanyi, Ber. **52**, 1792 (1919).

XXVIII

iso-PROPYL THIOCYANATE

$$(CH_3)_2CHBr + NaSCN \rightarrow (CH_3)_2CHSCN + NaBr$$

Submitted by R. L. SHRINER.
Checked by C. R. NOLLER.

1. Procedure

IN a 3-l. round-bottom flask, fitted with a very efficient mechanical stirrer (Note 1), a reflux condenser and a 500-cc. separatory funnel, are placed 445 g. (5.5 moles) of sodium thiocyanate (Note 2) and 1250 cc. of 90 per cent ethyl alcohol. The stirrer is started and the mixture is heated to boiling. Then 615 g. (5 moles) of isopropyl bromide is added slowly during the course of one hour. The mixture is refluxed with stirring for six hours. At the end of this time the precipitated sodium bromide is removed by filtration and washed with 250 cc. of 95 per cent alcohol. As much of the alcohol as possible is then removed by distillation on the steam bath. To the residue in the flask is added 500 cc. of water and the upper layer of isopropyl thiocyanate is separated. The aqueous layer is extracted with two 100-cc. portions of ether (Note 3). The ether extracts are added to the crude thiocyanate and the combined product is dried over anhydrous sodium sulfate (Note 4). The dried material is fractionated twice from a modified Claisen flask with a 25-cm. (10-in.) fractionating column (Org. Syn. **1**, 40). The following fractions are collected: up to 60°; 60–100°; 100–130°; 130–146°; and 146–151°. The latter fraction contains the pure product. The yield is 320–345 g. (63–67 per cent of the theoretical amount). By redistilling the alcohol that was removed on the steam bath through an efficient fractionating column (Note 5) until all the

alcohol is removed (Note 6), separating the water and distilling, there is obtained an additional 55–65 g. of product boiling at 146–151°. The total yield is 385–400 g. (76–79 per cent of the theoretical amount). On redistillation of the combined fractions boiling at 146–151°, practically the entire amount distils at 149–151°.

2. Notes

1. A vigorous mechanical stirrer must be used to prevent the precipitated sodium bromide from settling to the bottom and causing bumping.

2. A technical grade of sodium thiocyanate was used. Potassium thiocyanate does not possess any advantages over the sodium salt.

3. If benzene is used to extract the aqueous layer, three fractionations are necessary to obtain the same yields.

4. The sodium sulfate does not remove the water entirely and in the subsequent fractionation the water layer should be removed by means of a separatory funnel wherever it appears.

5. An eight-bubbler fractionating column of the type described by Clarke and Rahrs [1] was used.

6. Distillation was continued until water began to appear in the lowest bubbler.

3. Methods of Preparation

Isopropyl thiocyanate has been prepared by the action of isopropyl iodide on potassium thiocyanate.[2]

[1] Clarke and Rahrs, Ind. Eng. Chem. **18**, 1092 (1926).
[2] Henry, Ber. **2**, 496 (1869); Gerlich, Ann. **178**, 80 (1875).

XXIX

THIOBENZOPHENONE

$$CH_3CH_2ONa + H_2S \rightarrow C_2H_5OH + NaSH$$

$$C_6H_5CCl_2C_6H_5 + 2NaSH \rightarrow C_6H_5CSC_6H_5 + 2NaCl + H_2S$$

Submitted by H. STAUDINGER and H. FREUDENBERGER.
Checked by ROGER ADAMS and E. H. WOODRUFF.

1. Procedure

AN alcoholic solution of sodium hydrosulfide is prepared by dissolving 4.6 g. of sodium (0.2 mole) in 150 cc. of absolute alcohol and saturating the solution with dry hydrogen sulfide.

In a 3-l. three-neck flask, equipped with a mechanical stirrer and a reflux condenser, is placed 25 g. (0.11 mole) of benzophenone dichloride (Note 1). An inert atmosphere is obtained by passing carbon dioxide through the flask. The sodium hydrosulfide solution is added slowly (Note 2). A vigorous reaction occurs and it is controlled by cooling. The solution becomes deep blue in color.

After standing for one-half hour, water is added and the solution is extracted with ether. The ether solution is dried over calcium chloride and the ether is distilled. The residue is distilled under reduced pressure in an atmosphere of carbon dioxide (Note 3). Thiobenzophenone boils at 174°/14 mm.; it distils as a blue oil which, if pure and dry, forms beautiful blue crystals on cooling. The yield of crude product is 10–12.5 g. (50–63 per cent of the theoretical amount) (Note 4).

This product is approximately 75 per cent pure and is purified further by recrystallization from petroleum ether (b. p. 70–90°). The yield of purified product melting at 53–54° is 8.4–9.9 g. (42–49 per cent of the theoretical amount).

For preservation, the thiobenzophenone is sealed in a glass tube with dry carbon dioxide and placed in the dark.

2. Notes

1. The benzophenone dichloride was prepared by heating equivalent molecular quantities of benzophenone and phosphorus pentachloride to 145–150° for two hours and then fractionating the mixture under reduced pressure. The product used for this preparation boiled at 201–202°/35 mm.

2. It is necessary to have an excess of the chloride present at all times in order to prevent the formation of dibenzohydryl-disulfide, due to reduction of the thioketone with the hydrosulfide. If the chloride is added to the sodium hydrosulfide solution, a 70 per cent yield of the pure disulfide is obtained and no thioketone is formed.

3. All the operations in the purification should be done very quickly and out of contact with the air as much as possible.

4. Larger runs using 100 g. of benzophenone dichloride gave the same percentage yields of product.

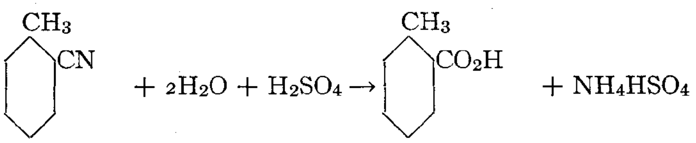
3. Methods of Preparation

Thiobenzophenone has been prepared by the action of thiophosgene on benzene in the presence of aluminum chloride;[1] by the action of phosphorus pentasulfide on benzophenone;[2] by the action of alcoholic potassium sulfide on benzophenone dichloride;[3] by treating benzophenone dichloride with an alcoholic solution of sodium hydrosulfide;[4] and by the action of thioacetic acid on benzophenone dichloride.[5]

[1] Bergreen, Ber. **21**, 341 (1888).
[2] Gattermann, Ber. **28**, 2877 (1895).
[3] Gattermann and Schulze, Ber. **29**, 2944 (1896).
[4] Staudinger and Freudenberger, Ber. **61**, 1577 (1928).
[5] Schönberg, Schültz, and Nickel, Ber. **61**, 1378 (1928)

XXX

o-TOLUIC ACID



Submitted by H. T. Clarke and E. R. Taylor.
Checked by C. S. Marvel and W. W. Moyer.

1. Procedure

In a 5-l. flask, equipped with a mechanical stirrer, a reflux condenser and a separatory funnel, is placed 3 kg. of 75 per cent sulfuric acid (sp. gr. 1.67). The solution is heated to about 150°, the stirrer is started and 1 kg. (8.55 moles) of *o*-tolunitrile (Org. Syn. **4**, 69) is added during the course of two hours. The temperature is maintained at 150–160° and the mixture is stirred for two hours after the addition of the nitrile is complete. The temperature is then raised to 190° and stirring is continued for another hour. Usually some crystalline material appears in the condenser at this stage. The reaction mixture is cooled, poured into ice water and filtered. The crude material is dissolved in an excess of 10 per cent sodium hydroxide solution (Note 1), filtered hot and the filtrate acidified with dilute sulfuric acid. The product is collected on a Büchner funnel, dried and recrystallized from about 3 l. of benzene (Note 2). The yield is 930–1030 g. (80–89 per cent of the theoretical amount) of a product which melts at 102–103° (Note 3).

2. Notes

1. Any insoluble material which separates on conversion into the sodium salt is toluamide, which may be isolated. The appearance of this substance indicates too short a period of heating or too low a temperature.

The reaction can be stopped readily so that a considerable quantity of the amide is produced. The crude amide is purified by recrystallization from water to give a product melting at 139–140°.

2. An additional amount of pure *o*-toluic acid may be obtained by distilling the benzene mother liquor to a small volume and allowing to cool.

3. *p*-Toluic acid (m.p. 178°) may be obtained from *p*-tolunitrile by the same process and in the same yields. This acid is less soluble in benzene and about 9 l. is needed for recrystallization.

3. Methods of Preparation

o-Toluic acid has been prepared by heating 1,3-naphthalene disulfonic acid, 1,3-dihydroxynaphthalene, 1-naphthol-3-sulfonic acid, or 1-naphthylamine-3-sulfonic acid with sodium hydroxide;[1] by reduction of phthalide with hydriodic acid and phosphorus;[2] by electrolytic oxidation of *o*-xylene;[3] by oxidation of *o*-xylene with dilute nitric acid;[4] by catalytic hydrogenation of phthalic anhydride;[5] and by hydrolysis of *o*-tolunitrile with 75 per cent sulfuric acid.[6]

[1] Ger. pat. 79,028 [Frdl. **4**, 147 (1899)]; Friedlander and Rüdt, Ber. **29**, 1611 (1896).
[2] Hessert, Ber. **11**, 238 (1878); Racine, Ann. **239**, 72 (1887).
[3] Fichter and Rinderspacher, Helv. Chim. Acta, **10**, 41 (1927).
[4] Fittig and Bieber, Ann. **156**, 242 (1870).
[5] Willstätter and Jaquet, Ber. **51**, 771 (1918).
[6] Cahn, Ann. **240**, 280 (1887).

XXXI

TRIETHYL CARBINOL

$$C_2H_5Br + Mg \rightarrow C_2H_5MgBr$$

$$3C_2H_5MgBr + (C_2H_5O)_2CO \rightarrow (C_2H_5)_3COMgBr + 2C_2H_5OMgBr$$

$$(C_2H_5)_3COMgBr + H_2O \rightarrow (C_2H_5)_3COH + Mg(OH)Br$$

Submitted by W. W. Moyer and C. S. Marvel.
Checked by Frank C. Whitmore and D. J. Loder.

1. Procedure

In a 3-l. three-neck flask, fitted with a mechanical stirrer, a 500-cc. separatory funnel and an efficient reflux condenser to which a calcium chloride tube is attached, are placed 107 g. (4.4 moles) of magnesium turnings and 800 cc. of anhydrous ether. The reaction is started by adding 5 cc. (7 g.; 0.07 mole) of ethyl bromide (Note 1) without stirring. The stirrer is started and a solution of 480 g. (4.4 moles) of ethyl bromide in 1 l. of anhydrous ether is added as rapidly as the refluxing of the ether allows. The addition requires about two hours (Note 2). The reaction is practically complete when all of the halide has been added, but stirring should be continued for fifteen minutes longer.

A solution of 156 g. (1.32 moles) of diethyl carbonate (Note 3) in 200 cc. of ether is added to the Grignard reagent, with rapid stirring, over a period of approximately three hours. The reaction is vigorous and the ether refluxes continually. After all of the diethyl carbonate has been added, the flask is heated on a water bath and stirring is continued for another hour.

The reaction mixture is hydrolyzed by pouring, it with frequent shaking, into a 5-l. round-bottom flask containing 1500 g.

of cracked ice and a solution of 300 g. of ammonium chloride in 600 cc. of water. The ether layer is separated in a large separatory funnel and the aqueous residue is extracted with two 500-cc. portions of ether (Note 4).

The ether is distilled from the combined extracts and the crude triethyl carbinol is dried with 10 g. of anhydrous potassium carbonate. The alcohol is then distilled at atmospheric pressure, and the portion (80–90 g.) boiling at 139–142° is collected. The low-boiling distillate is treated with 5 g. of anhydrous potassium carbonate, filtered and redistilled, whereby another portion (about 25 g.) of triethyl carbinol boiling at 139–142° is obtained. The process is repeated once, or twice if necessary, and an additional 20 g. is collected (Note 5). The total yield is 125–135 g. (82–88 per cent of the theoretical amount) (Note 6). Triethyl carbinol is a viscous liquid with a penetrating, camphor-like odor.

2. Notes

1. The ethyl bromide used in this preparation was dried over calcium chloride and then distilled from phosphorus pentoxide. The fraction boiling at 38–39° was collected.

2. The time of addition may be decreased by cooling the flask externally. A towel is folded in a narrow strip and wrapped about the flask above the ether line, and cracked ice is packed on top of the flask. This arrangement allows the ether vapor to be condensed without appreciable cooling of the reaction mixture.

3. The commercial "99 per cent" ester was washed with a 10 per cent solution of sodium carbonate, then with a saturated solution of calcium chloride and finally with water. After a short treatment with anhydrous calcium chloride, the ester was distilled and the portion boiling at 125–126° was collected and used in this preparation. It is not advisable to allow diethyl carbonate to stand over anhydrous calcium chloride for longer than a day, since it enters in combination with the calcium chloride.

4. The ether used for extraction may be obtained by distilling the ether from the triethyl carbinol solution.

5. In checking this preparation the first drying was allowed to continue for fifteen hours. The first fractionation of the carbinol yielded 122 g., the second 10 g., and the third yielded none.

6. The preparation of homologous trialkyl carbinols by use of the Grignard reagent and diethyl carbonate was found to be very satisfactory. The following compounds were prepared: tri-*n*-propyl carbinol (b. p. 89–92°/20 mm.) in 75 per cent yield; tri-*n*-butyl carbinol (b. p. 129–131/20 mm.) in 84 per cent yield; tri-*n*-amyl carbinol (b. p. 160–164°/19 mm.) in 75 per cent yield; and tri-*n*-heptyl carbinol (b. p. 195–200°/6 mm.) in 72 per cent yield.

3. Methods of Preparation

Triethyl carbinol has been prepared by the action of zinc on a mixture of ethyl iodide and diethyl ketone;[1] by the action of magnesium on ethyl bromide in diethyl ketone solution;[2] as a by-product in the reaction between ethylmagnesium bromide and carbon oxysulfide;[3] by the action of ethylmagnesium bromide on ethyl propionate;[4] by the action of ethylmagnesium bromide on ethyl chloroformate;[5] and by the action of ethylmagnesium bromide on ethyl cyanoformate.[6]

[1] Barataeff and Saytzeff, J. prakt. Chem. (2) **34**, 463 (1886).
[2] Kipping and Davies, J. Chem. Soc. **99**, 298 (1911).
[3] Weigert, Ber. **36**, 1009 (1903).
[4] Schreiner, J. prakt. Chem. (2) **82**, 295 (1910).
[5] Mazurewitsch, J. Russ. Phys.-Chem. Soc. **42**, 1582 (1910) [Chem. Zentr. **1911**, II, 1500].
[6] Bruylants, Bull. soc. chim. Belg. **33**, 529 (1924).

APPENDIX

LATER REFERENCES TO PREPARATIONS IN THE PRECEDING VOLUME

(The following references are to methods of possible preparative value that have been recently described. The numbers in parentheses following the name of the compound refer to the volume and page of Organic Syntheses.)

Durene (10, 32):

By recrystallization of crude durene (obtained substantially as described in Organic Syntheses) four times from alcohol and finally from benzene. SMITH and MACDOUGALL, J. Am. Chem. Soc. **51**, 3001 (1929).

Hexamethylbenzene (10, 35):

By the action of sulfuric acid upon pentamethylbenzene, prehnitene being formed simultaneously. SMITH and LUX, J. Am. Chem. Soc. **51**, 2997 (1929).

Oxalic Acid (Anhydrous) (10, 78):

By distilling a mixture of hydrated oxalic acid and toluene. JOHNSON and PARTINGTON, J. Chem. Soc. **1930**, 1510.

ADDITIONS AND CORRECTIONS FOR THE PRECEDING VOLUME

(The numbers in parentheses following the name of a compound, refer to a volume and page of Organic Syntheses.)

Ethyl Fumarate (10, 48):

The diagram (p. 49) of the apparatus used in this preparation is in error in the following points:

(1) Tube A should be a coarse capillary; in the diagram it is of a larger bore than the distilling column K.

(2) Tube A should barely dip into the mercury in B; in the diagram it is above the surface of the mercury.

(3) The top of the separatory funnel F should have a one-hole rubber stopper; in the diagram funnel F is open to the air, therefore, no pressure head is furnished by the liquid in G as should be.

(4) Thermometer T should not touch the bottom of flask J.

***m*-Nitroacetophenone** (10, 74):

No reference was given to a detailed paper by R. Camps, Arch. d. Pharm. **240**, 1 (1902). This author adds the acetophenone to ten times its weight of fuming nitric acid at temperatures of −10 to +20°. At the lower temperature a 96 per cent yield of nitroacetophenones was obtained, consisting of 45 per cent of the ortho derivative and 55 per cent of the meta.

Mr. W. W. Hartman (Eastman Kodak Company) has stated that larger runs of *m*-nitroacetophenone than those described in the procedure can be carried out if the beaker is surrounded with carbon dioxide and solid carbon dioxide is added directly to the reaction mixture.

SUBJECT INDEX

(This Index Comprises Material from Volumes X and XI of this Series)

(Names in small capital letters refer to the titles of preparations which are given in full detail. A number in ordinary bold face type denotes the volume. A number in bold face italics refers to a page which gives preparative directions for a substance formed either as principal product or as a by-product, or to a product which has been prepared by a method analogous to the one given. Other numbers in ordinary type indicate the page on which the compound is mentioned in connection with other preparations.)

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PREFACE TO VOLUME XI

SINCE the revised collection of the material in the first nine volumes of this series is soon to appear, no reference to new methods and no corrections for the preparations in these earlier volumes are included here. The index in this volume includes the material in Volume X but not that in the earlier volumes.

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